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Donald S. Prater — Donald S. Prater
Name (Print) Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	Raymond J. Wong	)	Examiner: Krishnan S. Menon
Application No.:	09/996,505	)	Group Art Unit: 1723
Filed:	November 28, 2001	)	Confirmation No.: 2941
Docket No.:	3192-002	)	Customer No.: 33432

For: CARTRIDGES USEFUL IN CLEANING DIALYSIS SOLUTIONS

APPELLANT'S SUPPLEMENTAL BRIEF ON APPEAL

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

November 22, 2004

Sir:

This is supplemental to and a reinstatement of the previous appeal to the Board of Patent Appeals and Interferences (hereinafter "the Board") filed July 2, 2004 , and now is in response to the Office Action dated August 20, 2004, rejecting claims 1-11, 13-38, and 50-61 in the above-identified application. Claims 40, 42-46, 48, and 49 are withdrawn. No serious burden exists to examine all of the claims at this time. Furthermore, while claims 40, 42-46, 48, and 49 are withdrawn, the appellant believes that with the allowance of the independent claims, these claims should be allowable as well because they relate to method claims that are using the sorbent cartridge of the independent claims that have been examined. No claims stand allowed. The appealed claims and the rest of the pending claims are set forth in the attached Claims Appendix.

I. REAL PARTY IN INTEREST

The real party in interest, besides the named inventor, is Renal Solutions, Inc.

II. RELATED APPEALS AND INTERFERENCES

No other appeal or interference which would directly affect or be directly affected by or have a bearing on the Board's decision in this appeal is known to the appellant or the appellant's legal representative.

III. STATUS OF CLAIMS

The claims pending in the application are claims 1-11, 13-38, 40, 42-46, and 48-61. Claims 12, 39, 41, and 47 are canceled.

Claims 40, 42-46, 48, and 49 were withdrawn due to a restriction requirement. However, in a final Office Action dated December 3, 2003, the Examiner indicated that claims 40, 42-46, 48, and 49 would be allowable if the product claims are found allowable.

A copy of the claims on appeal and the rest of the pending claims can be found in the attached Claims Appendix.

IV. STATUS OF AMENDMENTS

In response to the final Office Action dated December 3, 2003, a Request for Reconsideration dated May 3, 2004, was filed. No amendments were made. An Advisory Action dated May 26, 2004 was received.

The appellant then filed an Appeal Brief dated July 2, 2004. In response, the Examiner issued an Office Action dated August 20, 2004 with five new, but similar, rejections.

V. SUMMARY OF CLAIMED SUBJECT MATTER

There is always a continuing effort to improve cartridges useful in cleaning dialysis solutions. Prior to the present invention, the REDY cartridge was used for certain dialysis therapy. While this cartridge had a good efficacy and safety record, the REDY cartridge can produce a variation of dialysate composition and pH during the treatment with a continuous release of Na^+ by the cartridge. Thus, the REDY dialysis therapy had to provide several dialysate prescriptions to balance the Na^+ level in the patient for the correction of hyper and hyponatremia. The current method of making ZrP for the REDY cartridge is titrating acid ZrP (H^+ZrP) to the pH range 6.25 - 6.45 in a NaCl/NaAc buffer to produce Na^+H^+ZrP with high Na^+ content. This will trigger the Na^+ release especially in acetate or lactate dialysate with low buffer capacity and at low pH. Thus, the ZrP quality made for the REDY cartridge may not be suitable for the peritoneal dialysis (PD) fluid regeneration application. (*See* pages 6 and 7 of the present application). Another disadvantage of using the previously designed REDY cartridge for PD treatment is that it may produce a continuous rise of Na^+ concentration of up to 170 mEq/l due to dominate Na^+ exchange throughout the treatment. In addition, an initial dip of Na^+, HCO_3, and pH may occur due to short time H^+ exchange. (*See* page 8, lines 6-10 of the present application).

The claimed invention contains a number of features that are listed at page 8, line 17 - page 9, line 9 that are useful in the regeneration or purification of solutions containing waste products in dialysis solutions. Preferably, the solutions are dialysis solutions such as peritoneal dialysis solutions, or other dialysis solutions such as those used in hemodialysis.

As set forth in independent claim 1 on appeal, the claimed invention relates to a sorbent cartridge that contains at least two layers. (*See*, e.g., Figs. 4-6 and page 20, lines 6-8 of the present application). One of the layers includes at least sodium zirconium carbonate (SZC) in the

sorbent cartridge. (*See*, e.g., page 9, lines 9 and 10; page 21, lines 19 and 20; and page 22, lines 11-14 of the present application). The characteristics of a preferred SZC of the claimed invention are described, for instance, in detail at page 12, lines 15-23, of the present application.

Claim 2 is dependent on claim 1 and recites that one of the layers consists essentially of sodium zirconium carbonate. (*See*, e.g., page 9, lines 9 and 10 and Fig. 4 of the present application).

Claim 3 is dependent on claim 1 and recites that the sorbent cartridge comprises zirconium phosphate. (*See*, e.g., page 9, line 10 of the present application).

Claim 4 is dependent on claim 3 and recites that the zirconium phosphate is present as a layer in the sorbent cartridge. (*See*, e.g., page 21, lines 20-22 of the present application). The zirconium phosphate (ZrP) can include the characteristics that are described, for instance, in detail at page 14, line 18 - page 15, line 2 of the present application.

As set forth in independent claim 11 on appeal, the claimed invention relates to a sorbent cartridge that contains an alkali metal-Group IV B metal carbonate. (*See*, page 9, lines 11 and 12 and lines 18 and 19; page 10, lines 4-6; and page 11, lines 18 and 19 of the present application). The alkali metal-Group IV B metal carbonate is present as a layer in the sorbent cartridge. (*See*, e.g., page 9, lines 13-15 of the present application).

Claim 16 is dependent on claim 15 and recites that the layers in the sorbent cartridge have the following order: SZC, ZrP, alumina, alumina supported urease, and granular activated carbon layer. (*See*, e.g., page 22, lines 11-20 of the present application). Furthermore, according to page 22, lines 21-25, of the present application, preferably, one or more filter pads can be located throughout the sorbent cartridge to ensure that the integrity of the layers is maintained during operation.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed on appeal by the Board of Patent Appeals and Interferences are:

A. The Examiner's rejection of claims 1, 3-9, 11, 13-16, 19-25, 29-38, and 50-61 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al. (U.S. Patent No. 4,650,587).

B. The Examiner's rejection of claim 2 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Smakman et al. (U.S. Patent No. 4,542,015).

C. The Examiner's rejection of claims 26-28 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Potts (U.S. Patent No. 5,234,603).

D. The Examiner's rejection of claims 17 and 18 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Marantz et al. (U.S. Patent No. 3,669,880).

E. The Examiner's rejection of claim 10 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Tawil et al. (U.S. Patent No. 4,025,608).

VII. ARGUMENTS

A. The Examiner's rejection of claims 1, 3-9, 11, 13-16, 19-25, 29-38, and 50-61 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al. (U.S. Patent No. 4,650,587).

1. The Examiner's rejection.

At page 2 of the Office Action dated August 20, 2004, the Examiner now rejects claims 1, 3-9, 11, 13-16, 19-25, 29-38, and 50-61 under 35 U.S.C. §103(a) as being unpatentable over the appellant's own disclosure of the REDY cartridge in view of Polak et al. According to the Examiner, the Applicant's disclosure of the REDY cartridge describes a sorbent cartridge having several layers of sorbents, such as zirconium phosphate (ZrP), zirconium hydrous oxide (HZO), and activated carbon. The Examiner indicates that the REDY cartridge does not teach sodium zirconium carbonate (SZC) as one of the layers. However, the Examiner asserts that Polak et al. describes a capsule having SZC as a phosphate ion absorber. Thus, the Examiner concludes that it would have been obvious to one of ordinary skill in the art, at the time of invention, to use the teachings of Polak et al. in the REDY cartridge.

For the following reasons, the Examiner's rejection should be reversed.

As argued below:

Claims 1, 11, 14, 15, 20, 37, 38, and 50-57 stand or fall together;

Claim 2 stands or falls on its own;

Claims 3, 5-10, 13, 30, 31, and 58-61 stand or fall together;

Claim 4 stands or falls on its own;

Claim 16-18 stand or fall together;

Claim 19 stands or falls on its own;

Claim 21 stands or falls on its own;

Claims 22-25 stand or fall together;

Claims 26-28 stand or fall together;

Claim 29 stands or falls on its own; and

Claims 32-36 stand or fall together.

2. The Appellant's Reply to the Examiner's rejection of claims 1, 3-9, 11, 13-16, 19-25, 29-38, and 50-61 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al. (U.S. Patent No. 4,650,587).

Throughout the Office Action, the Examiner refers to the "applicant's own disclosure of prior art." In reviewing the rejections, the Examiner specifically states that the applicant's disclosure of prior art, the REDY cartridge, describes sorbents in layers in a cartridge. *See* page 3 of the final Office Action dated December 3, 2003. The appellant provided to the Examiner, by way of an Information Disclosure Statement, two detailed booklets entitled "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are dated 1993 and set forth the configuration of the REDY cartridge. Most importantly, as shown in these booklets, this chemical field is very complex. Reference throughout this Appeal Brief to the "REDY cartridge" is with reference to the REDY cartridge as set forth in these booklets, as well as Figures 1 and 8 in the present application.

a) The patentability of claims 1, 11, 14, 15, 20, 37, 38, and 50-57.

In terms of the claims at issue, the following summary is provided:

Claim 1 recites a sorbent cartridge comprising at least two layers, wherein one of the layers comprises at least sodium zirconium carbonate in the sorbent cartridge.

Claim 11 recites a sorbent cartridge comprising an alkali metal-Group IV B metal carbonate, wherein the alkali metal-Group IV B metal carbonate is present as a layer in the sorbent cartridge.

Claim 14 is dependent on claim 1 and recites that the sorbent cartridge further includes alumina, alumina supported urease, granular activated carbon, or combinations thereof. Claim 15 recites that the alumina, alumina supported urease, and granular activated carbon of claim 14 are each present as separate layers in the sorbent cartridge.

Claim 20 is dependent on claim 1 and recites that the sodium zirconium carbonate satisfies the ANSI/AAMI RD-5-1992 standard on extractable toxic impurities.

Claim 37 is dependent on claim 11 and recites that the sorbent cartridge further comprises a chlorine removal material.

Claim 38 is dependent on claim 11 and recites that the materials are present as two or more layers in the cartridge.

Claim 50 recites an apparatus for conducting dialysis comprising the sorbent cartridge of claim 1 and a dialyzer in fluid communication with the cartridge wherein spent dialysis fluid passes from the dialyzer to and through the cartridge.

Claim 51 is dependent on claim 50 and recites that the spent dialysis fluid is spent hemodialysis fluid.

Claims 52 and 57 are dependent on claims 50 and 1, respectively, and recite that the spent dialysis fluid is restored to the original balance of the Na^+ and HCO_3^- contents found in a fresh dialysate, and that the cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in a fresh dialysate, respectively.

Claim 53 is dependent on claim 50 and recites that the dialyzer is in fluid communication

with the blood of a patient.

Claim 54 is dependent on claim 53 and recites that the Na^+ and HCO_3^- balance in the blood is restored to levels found in a healthy patient without renal problems.

Claim 55 is dependent on claim 50 and recites that the spent dialysis fluid is spent dialysate fluid obtained from a dialyzer wherein spent peritoneal dialysis fluid is passed through the dialyzer and cleaned by fresh dialysate fluid.

Claim 56 recites a dialysis system including a sorbent cartridge and a source of spent peritoneal dialysis solution, wherein the source of the spent peritoneal dialysis solution is in fluid communication with the cartridge and wherein the spent peritoneal dialysis solution passes to and through the cartridge.

With respect to the REDY cartridge, as shown in Figures 1 and 8 of the present application, and as further shown in the booklets entitled "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," the REDY cartridge is a cartridge having a very specific arrangement of chemical layers. As shown in Figure 1 of the present application, the REDY cartridge does not include any layer that contains sodium zirconium carbonate. The REDY cartridge disclosure provides no teaching or suggestion of substituting any one of these layers at all. Essentially, the Examiner is taking the position that the multi-layered cartridge of REDY containing a layer of ZrP is replaced with the MGP of Polak which includes SZC. However, no motivation is provided in either reference to do so.

Polak et al. relates to a particulate magnesium phosphate product (MGP) and to a method for removing ammonia from aqueous solutions. According to Polak et al., MGP (and not SZC) can be utilized as a replacement for ZrP materials, which are used to remove ammonia produced by enzymatic hydrolysis of urea in recirculating dialysis systems utilizing disposable cartridges.

Polak et al. does not teach or suggest that the SZC is present as a layer in a sorbent cartridge. SZC is never used alone in Polak et al. Polak et al. requires that SZC be used with MGP. For example, Polak et al. at Figure 2 and column 6, lines 9-11, only describes a mixture of MGP and SZC components in a pouch. There is absolutely no teaching or even a suggestion to use SZC as a layer with other layered materials. A mixture of MGP and SZC in a pouch does not constitute a layer in a cartridge and most certainly does not constitute an SZC layer. Therefore, contrary to the Examiner's statements, Polak et al. does not teach or suggest using a layered structure and never once teaches ZrP with SZC. Thus, the non-layered pouch of Polak would provide no motivation to replace a layer in the layered structure of REDY.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system, Polak et al. relates to an encapsulated capsule for oral consumption. See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the two references would not be combinable for this reason as well.

Further, the use of a layer of SZC has an important function, and is not a cosmetic difference. In one example of the present application, the SZC layer is, in part, a phosphate adsorbent, which can remove phosphate from a renal disease patient for the treatment of hyperphosphatemia. Preferably, SZC produces bicarbonates that can be delivered to a patient for correcting the metabolic acidosis. Furthermore, the SZC layer, preferably, buffers the acidity of the dialysate caused by the lattice hydrogen ions of ZrP and hydrous zirconium oxide (HZO), which will otherwise decompose the bicarbonate dialysate and lower the bicarbonate level of the patient.

Additionally, claim 1 of the present application specifically recites two layers, one of which is SZC. Polak does not show two layers at all.

Furthermore, the REDY cartridge includes layers, whereas the cartridge of Polak et al. does not. How the REDY cartridge can be combinable with Polak et al. is not seen.

Further, one cannot simply replace one of the layers in the REDY cartridge with the material of Polak et al. and reasonably expect success. At best, this is an improper obvious to try standard.

The Examiner cannot simply pick and choose layers and design a cartridge to reject the claimed invention when the prior art does not provide this motivation. The Examiner is improperly using hindsight to arrive at this conclusion. The REDY cartridge and Polak et al. do not suggest such a substitution.

With respect to the Examiner's argument that having the material in a pouch does not make it any less layered, at page 3 of the final Office Action dated December 3, 2003, the Examiner specifically states that Polak et al. does not disclose layers comprising SZC. Further, claim 1 of the present application specifically recites two layers, one of which is SZC. Where are the two layers in Polak et al.? Polak does not show two layers at all. Certainly, the Examiner cannot point to any part of Polak et al to support the Examiner's position. The Examiner, at page 5 of the final Office Action, further emphasizes that Polak et al. does not describe layers comprising SZC by stating that Polak et al. does not teach how the absorbents are structured in the cartridge.

With respect to claims 14, 15, 37, and 38, simply because a similar general material may be mentioned in a reference does not mean that the compound has the same properties. There has to be a technical basis for concluding obviousness or for asserting inherency. It is not enough for the Examiner to simply say that the same material is automatically used when clearly the present

invention, especially the claims of the present application, set forth precise chemical properties or amounts that are clearly not taught or suggested in the cited art. The Examiner at times asserts that certain characteristics are "a material property," and therefore concludes obviousness. However, a material property that is not taught or suggested in the cited art is clearly reason enough for patentability. There are many patents that would attest to this standard.

In addition, with respect to claim 20, wherein the Examiner states that the material of Polak et al. would satisfy the ANSI/AAMI standard, again, the Examiner has not even shown that the material is the same and therefore, one cannot conclude that it would satisfy such a requirement. This is especially true when the material used in Polak et al. is not even used as a layered structure.

With respect to the Examiner's rejection of claim 29, wherein the Examiner asserts that the "[d]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art," first of all, the appellant respectfully points out that the claims being rejected are product claims and not process claims. Thus, the Examiner's argument does not apply. In addition, the sorbent cartridge claims are not "a known process" or a known product. As pointed out above, clearly Polak et al. does not teach or suggest these amounts which are present in a layered structure. Since the purpose and design of Polak et al. is not even close to the claimed invention, one cannot assert that this is a mere optimization issue. Clearly, these amounts have relevance as shown in the present application and the relevance of these amounts are clearly not taught or suggested in Polak et al. or by the REDY cartridge.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al. does not render the claimed invention unpatentable, and the rejection of claims 1, 11, 14, 15, 20, 37, 38, and 50-57 should be reversed.

b) The patentability of claims 3, 5-9, 13, 30, 31, and 58-61.

Claim 3 is dependent on claim 1 and recites that the sorbent cartridge further includes a zirconium phosphate.

Claim 5 is dependent on claim 3 and recites that the zirconium phosphate comprises a H^+ content of from about 1.4 to about 2.0 wt%; a Na^+ content of from about 4 to about 6 wt%; a ZrO_2 wt% of from about 34 wt% to about 37 wt%; a PO_4 wt% of from about 41 wt% to about 43 wt%; and a H_2O wt% of from about 14 wt% to about 18 wt%, based on the weight of the zirconium phosphate.

Claim 6 is dependent on claim 3 and recites that the zirconium phosphate has at least one of the following characteristics: (a) an adsorption capacity for ammonia of from about 20 mg NH_4-N/gm ZrP to about 45 mg NH_4-N/gm ZrP; an adsorption capacity for Ca^{2+} of from about 2 mEq Ca^{2+}/gm ZrP to about 7 mEq Ca^{2+}/gm ZrP; an adsorption capacity for Mg^{2+} of from about 1 mEq Mg^{2+}/gm ZrP to about 5 mEq Mg^{2+}/gm ZrP; and an adsorption capacity for toxic heavy metals of from about 3 mEq HM/gm ZrP to about 9 mEq HM/gm ZrP; (b) a Na^+ content of from about 1.8 mEq Na^+/gm ZrP to about 3 mEq Na^+/gm ZrP at a pH of from about 5.5 to about 6; (c) a minimum leachable PO_4^{3-} of less than about 0.05 mg PO_4^{3-}/gm ZrP; or (d) satisfying ANSI/AAMI RD-5-1992 standard on extractable toxic impurities.

Claims 7 and 8 are dependent on claim 5, and claim 9 is dependent on claim 3, and recite that the zirconium phosphate has no residual sulfate or chloride; has less than 0.01% sulfate, chloride, or both; and has a pH of from about 6 to about 7, respectively.

Claim 13 is dependent on claim 11 and recites that the sorbent cartridge further includes a Group IV B metal phosphate.

Claim 30 is dependent on claim 29 and recites that the cartridge further includes zirconium phosphate in an amount of from about 300 grams to about 1900 grams.

Claim 31 is dependent on claim 30 and recites that the cartridge further includes alumina in the amount of from about 100 grams to about 500 grams, immobilized enzyme in an amount of from about 100 grams to about 300 grams, and activated carbon or other adsorbent in an amount of from about 100 grams to about 500 grams.

Claims 58 and 59 are dependent on claims 5 and 31, respectively, and recite that the cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in fresh dialysate, and that the cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in fresh dialysate, respectively.

Claims 60 and 61 are dependent on claims 3 and 4, respectively, and recite that the zirconium phosphate is further away from an inlet opening of the sorbent cartridge than the layer of sodium carbonate and SZC, respectively.

Polak et al. does not teach or suggest using a layered structure, and never once teaches or suggests the use of ZrP with SZC. Columns 5 and 6 of Polak et al., which the Examiner relies upon, only show the use of MGP mixed with SZC.

Polak et al. uses MGP with an SZC and discourages the use of ZrP. Polak et al. specially teaches that MGP is a replacement for ZrP. There is absolutely no teaching or suggestion in Polak et al. to use ZrP with SZC, especially in any layered configuration.

The layered structure of the claimed invention is based on the principle of adsorption column design to ensure high adsorption efficiency. A blended mixture of components, especially a blended mixture of ZrP and SZC, will not only cause a high level of phosphate leakage, but also can cause a rapid uncontrolled reaction that produces CO_2 gas.

Although the references cited in Polak et al., such as U.S. Patent No. 3,669,880, describe a cartridge having a ZrP layer, the references simply do not teach or suggest the use of an SZC layer

in combination with a ZrP layer. As stated above, Polak et al. even discourages the use of ZrP due to its disadvantages as mentioned at col. 3, lines 11-36; and col. 4, lines 38-48, and the references cited within Polak et al. Polak et al. further states that MGP is a replacement for ZrP. One skilled in the art would conclude that SZC can only be used in combination with MGP and not with ZrP. In addition, none of the references in Polak et al. shows the use of SZC as a layer.

Furthermore, the REDY cartridge, as stated above, relates to several layers of chemical materials. One of these layers is zirconium phosphate. There is no sodium zirconium carbonate layer in the REDY cartridge. The Examiner does not dispute this point. If one combines Polak et al. with the REDY cartridge, if this is possible, at best one skilled in the art would substitute the zirconium phosphate layer of the REDY cartridge, for instance, as shown in Figure 1 of the present application, with the magnesium phosphate product of Polak et al. As stated above, Polak et al. specifically states that the magnesium phosphate product of Polak et al. is a replacement for zirconium phosphate. Thus, if one combines Polak et al. with the REDY cartridge, one would replace the zirconium phosphate layer of the REDY cartridge with the magnesium phosphate product of Polak et al. which may contain sodium zirconium carbonate. If this is done, then by this combination, the REDY cartridge would not have any zirconium phosphate layer because it was replaced with the magnesium phosphate product of Polak et al. based on the Examiner's reasoning. In view of this, the REDY cartridge, even combined with Polak et al., cannot possibly teach or suggest a sorbent cartridge that contains both zirconium phosphate along with sodium zirconium carbonate as required by claim 3 of the present application. After all, the zirconium phosphate was replaced by the magnesium phosphate product of Polak et al. which may contain sodium zirconium carbonate. There are no exceptions to this replacement made in Polak et al. or in the patents referenced by Polak et al. The magnesium phosphate product of Polak et al. is an absolute

replacement for the zirconium phosphate.

Additionally, one skilled in the art, after reviewing the teachings of Polak et al. and the REDY cartridge, would not be motivated to replace the HZO layer of the REDY cartridge with SZC. Neither Polak et al. nor the REDY cartridge teaches or suggests such a substitution. In fact, based on the high level of phosphate leakage created by having a blended mixture of ZrP and SZC, one skilled in the art would prefer to use HZO instead of SZC.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system, Polak et al. relates to an encapsulated capsule for oral consumption. See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the two references would not be combinable for this reason as well.

With respect to the Examiner's rejection of claims 5-9, and 30 and the remaining rejected claims, clearly Polak et al. does not teach or suggest the amounts of the compounds recited in these claims or other characteristics which are present in a layered structure. Since the purpose and design of Polak et al. is not even close to the claimed invention, one cannot assert that this is a mere optimization issue. Clearly, these amounts have relevance as shown in the present application and the relevance of these amounts are clearly not taught or suggested in Polak et al. or by the Examiner's reliance on the REDY cartridge.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al. does not render the claimed invention unpatentable and the rejection of claims 3, 5-9, 13, 30, 31, and 58-61 should be reversed.

c) The patentability of claim 4.

Claim 4 recites that the zirconium phosphate of claim 3 is present as a layer in the sorbent cartridge.

With respect to claim 4, which recites that the zirconium phosphate is present as a layer in the sorbent cartridge along with a separate layer of sodium zirconium carbonate, again, Polak et al. specifically states that the magnesium phosphate product of Polak et al. is a complete replacement for zirconium phosphate. Therefore, if one somehow could combine Polak et al. with the REDY cartridge, for instance, as shown in Figure 1 of the present application, one would replace the zirconium phosphate layer of the REDY cartridge with the magnesium phosphate product of Polak et al. Thus, after this combination, there would be absolutely no zirconium phosphate layer present in the REDY cartridge. Therefore, claim 4 cannot possibly be obvious in view of this combination because claim 4 requires a zirconium phosphate layer and a sodium zirconium carbonate layer in the same sorbent cartridge.

Clearly, this rejection should be reversed as well.

d) The patentability of claim 16.

Claim 16 is dependent on claim 15 and recites that the layers have the following order: a) a sodium zirconium carbonate; b) a zirconium phosphate; c) an alumina; d) an alumina supported urease; and e) a granular activated carbon.

Claim 16 recites a specific order of layers which clearly is not taught or suggested in the cited references as admitted by the Examiner. It is important for the Board to recognize that the scope of the invention is determined by the language recited in the claims and not by the options provided in the specification. The Examiner cannot use the appellant's own disclosure for purposes of rejecting the claims. Furthermore, in addition to not teaching or suggesting the particular order of the layers recited in claim 16 of the present application, the REDY cartridge does not teach or

suggest an SZC layer as recited in claim 16 of the present application. Additionally, as stated above, Polak et al. does not teach or suggest a cartridge having layers. Furthermore, no motivation exists to separate the MGP and SZC mixture of Polak et al., to form the separated SZC into a layer, and to substitute one layer of the REDY cartridge with the formed SZC layer. Also, as indicated above, if Polak et al. is combined with the REDY cartridge, then the magnesium phosphate product of Polak et al. will replace the ZrP layer of the REDY cartridge, and result in no ZrP layer at all. Claim 16 requires a ZrP layer and a separate SZC layer.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system, Polak et al. relates to an encapsulated capsule for oral consumption. See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the two references would not be combinable for this reason as well.

With respect to the Examiner's reliance on *In re Ruff*, 118 U.S.P.Q. 340 (C.C.P.A. 1958), the appellant responds as follows. The Examiner relied on this decision to argue that the appellant's express recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist. In *In re Ruff*, the appellants in their search for tarnish inhibitors made the discovery that two different classes of complex organic chemical compounds were effective for that purpose, the amino and mercapto compounds. The chemists working for their assignee's competitor, carrying on the same research, discovered the effectiveness of the amino compounds first. Originally, the applicants recited both groups in a Markush claim. The Patent Office, solely for the reason that the appellants included both groups in one application, and even after deletion of the amino group in which the appellants lost the

race to their rival Schaeffer, decided that the appellants cannot have a patent on the detergents including the mercapto compounds because they are not patentable. According to the Patent Office, the mercapto compounds are not patentable because they are the "equivalents" of the amino compounds, which the appellants were not the first to invent and the appellants in their application stated that they were useful for the same purpose. Upon review, the Court of Customs and Patent Appeals concluded that actual equivalence is not enough to justify refusal of a patent on one member of a group when another member is in the prior art. The equivalence must be disclosed in the prior art or be obvious within the terms of Section 103. The only reason that the Patent Office used the applicants' own disclosure to reject the claims of Ruff et al. was because *In re Borcherdt et al.* became applicable when the appellants admitted in their application that the prior art amino group is equivalent to the mercapto compounds.

The present application never mentions that the REDY cartridge is equivalent to the cartridge of the claimed invention. In fact, at page 8 of the present application, the appellant distinguishes the present application from the REDY cartridge by stating that the REDY cartridge may produce a continuous rise of Na^+ concentration up to 170 mEq/l due to dominant Na^+ exchange throughout the treatment. In addition, an initial dip of Na^+. HCO_3 and pH may occur due to short time H^+ exchange. Thus, the present application has a completely different fact pattern from *In re Ruff* and *In re Borcherdt et al.* It is quite improper for the Examiner to use the appellant's own disclosure to reject the claimed invention. The Examiner has clearly not established a *prima facie* case of obviousness since the Examiner is not relying on any prior art to show what is obvious to one of ordinary skill in the art. Accordingly, the Examiner's use of the appellant's own disclosure for the purposes of rejecting the claims is in error.

The present invention relates to a complicated chemical sorbent cartridge which involves layers that contain various chemical materials which can affect each other. These layers, for instance, recited in claim 16, are not merely mechanical parts. The present invention is a chemical invention that involves the use of various chemical layers that, in a certain order, can provide various benefits as explained in the present application to regenerate or purify spent dialysis fluid. Unfortunately, the Examiner ignores the chemistry of the present application and simply believes that it would be proper to randomly pick and choose and re-arrange various layers to come up with the claimed invention when the prior art does not provide any motivation to make these substitutions, and the prior art does not teach or suggest that one would reasonably expect success in making such substitutions.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al. does not render the claimed invention unpatentable, and the rejection of claim 16 should be reversed.

e) The patentability of claim 19.

Claim 19 is dependent on claim 1 and recites that the sodium zirconium carbonate comprises from about 2 wt% to about 5 wt% Na^+; from about 44 wt% to about 50 wt% ZrO_2; from about 12 wt% to about 18 wt% CO_3^{2-}; and from about 30 wt% to about 40 wt% LOD, based on the weight of the sodium zirconium carbonate.

With respect to claim 19, the appellant respectfully points out that the SZC product set forth in Polak et al., as described at the top of column 6, has the formula $Na_{0.8\text{-}1.2}(ZrO_2)_1(CO_3)_{0.8\text{-}1.2}$.

On the other hand, this formula clearly would not be covered, for instance, by the SZC set forth in claim 19 of the present application.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge

disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system, Polak et al. relates to an encapsulated capsule for oral consumption. See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the two references would not be combinable for this reason as well.

Accordingly, for the reasons stated above, including the reasons set forth above with respect to claim 1, the REDY cartridge in view of Polak et al. does not render the claimed invention unpatentable, and the rejection of claim 19 should be reversed.

f) The patentability of claim 21.

Claim 21 is dependent on claim 1 and recites that the sodium zirconium carbonate satisfies at least one of the following characteristics: a phosphate adsorption having a minimum capacity of from about 30 to about 35 mg/PO_4-P/gm SZC; a minimum HCO_3^- content of from about 2 to about 4 mEq HCO_3^-/gm SZC; a leachable Na^+ content of from about 1.5 to about 2.0 mEq Na^+/gm SZC; or a pH range of titrated sodium zirconium carbonate of from about 6 to about 7.

With respect to claim 21, Polak et al. does not teach or suggest the characteristics of the sodium zirconium carbonate as recited in claim 21. The characteristics as recited in claim 21 lead to an effective and sufficient way to regenerate or purify spent dialysis fluid. Polak et al. does not provide any such characteristics and would not even appreciate the need for these characteristics because, as stated above, the importance of Polak et al. relates to magnesium phosphate. Polak et al. simply uses sodium zirconium carbonate as an extra component to mix with the magnesium phosphate. Polak et al. is not interested in using sodium zirconium carbonate in the same manner

as set forth in the sorbent cartridge of the present invention and therefore would not appreciate the characteristics useful in using sodium zirconium carbonate as a layer.

Furthermore, as discussed above, the REDY cartridge does not even teach or suggest the use of any sodium zirconium carbonate and therefore would not teach or suggest any characteristics of a sodium zirconium carbonate. Thus, even if Polak et al. is somehow combinable with the REDY cartridge, the subject matter of claim 21 is still not obvious in view of these references. Therefore, the Examiner's rejection should be reversed.

g) The patentability of claims 22-25.

Claim 22 is dependent on claim 1 and recites that the sorbent cartridge further includes hydrous zirconium oxide and claim 23 recites that the hydrous zirconium oxide in claim 22 is in the acetate form.

Claim 24 is dependent on claim 23 and recites that the sodium zirconium carbonate and the hydrous zirconium oxide are present in a weight ratio of about 1 to 1.

Claim 25 is dependent on claim 23 and recites that the sodium zirconium carbonate and the hydrous zirconium oxide are present in the same layer and are blended together.

As stated earlier, one skilled in the art, after reviewing the teachings of Polak et al. and the REDY cartridge, would not be motivated to replace the HZO layer of the REDY cartridge with an SZC layer. Neither Polak et al. nor the REDY cartridge teach or suggest such a substitution. Furthermore, there is absolutely no motivation to add an SZC layer to the REDY cartridge or substitute the HZO layer of the REDY cartridge with an SZC layer. Additionally, even if one skilled in the art, as suggested by the Examiner, would substitute the HZO layer of the REDY cartridge with an SZC layer, such a substitution would still not teach or suggest claims 22-25 of the present application. As recited in claims 22-25 of the present application, the sorbent cartridge of

the claimed invention, in addition to the SZC layer, includes a HZO layer. Substituting one layer for the other, as the Examiner suggest, would not teach or suggest having both an SZC layer and an HZO layer.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al. does not render the claimed invention unpatentable and the rejection of claims 22-25 should be reversed.

h) The patentability of claim 29.

Claim 29 is dependent on claim 1 and recites that the sodium zirconium carbonate is present in the cartridge in an amount of from about 100 grams to about 300 grams. As stated above, Polak et al. specifically states that the magnesium phosphate is a replacement for zirconium phosphate. In addition, Polak et al. states that a certain type of sodium zirconium carbonate can be used with the magnesium phosphate. However, other than a formula provided at column 6 of Polak et al., no other details are provided concerning the sodium zirconium carbonate. In fact, Polak et al. specifically states, after indicating that a specific sodium zirconium carbonate product can be present, "[h]owever, our primary interest is for the use of the MGP in a system to be ingested by uremic patients for the enteric elimination of urea." As stated, no other details concerning the amount of the sodium zirconium carbonate, and the like, are provided anywhere in Polak et al.

Claim 29, which is dependent on claim 1, recites a specific amount of the sodium zirconium carbonate that is present in a cartridge as a layer in the sorbent cartridge. As stated, first Polak et al. does not teach or suggest the use of any layer containing sodium zirconium carbonate alone or even with any other component. Second, Polak et al. does not describe any amounts of the sodium zirconium carbonate. Moreover, the amounts specified in claim 29 of the

present application would not be obvious or inherent in Polak et al. as the emphasis of Polak et al. is the magnesium phosphate product. Clearly, by reading Polak et al. alone or even combined with the REDY cartridge, one skilled in the art would not be able to find any teaching or even a suggestion on the amounts of the sodium zirconium carbonate that can be used in a sorbent cartridge as a layer. Again, the Examiner has not established a prima facie case of obviousness with respect to this subject matter. Accordingly, the subject matter of claim 29 is not taught or suggested by Polak et al. or the REDY cartridge alone or combined.

i) The patentability of claims 32-36.

Claim 32 recites a sorbent cartridge that is dependent on claim 1 and further comprises an immobilized enzyme material capable of enzymatic conversion of urea to ammonium carbonate, a cation exchange material in the sodium or hydrogen form, and anion exchange material in the Ac^-, HCO_3^-, Cl^-, or OH^- form, and an adsorbent capable of removing creatinine, uric acid, or both. Claim 33 is dependent on claim 32 and recites the additional presence of a chlorine removal material. Claims 34 and 35 are dependent on claims 32 and 33, respectively, and recite that the materials are present as two or more layers in the cartridge.

Also, claim 36, which is dependent on claim 11, recites the same language as claim 32, but is, as indicated, dependent on claim 11.

Unlike the subject matter of these claims, Polak et al., as indicated, only shows a mixture of MGP with an SZC, nothing else. There are no layers taught or even suggested in Polak et al. Furthermore, the REDY cartridge does not teach a sorbent cartridge that has a sodium zirconium carbonate layer or an alkali metal-Group IV B metal carbonate layer in combination with the components recited in claims 32-36. The Examiner has not explained how one skilled in the art would simply take a sodium zirconium carbonate layer and include it in the REDY cartridge

along with the other components recited in claims 32-36 and achieve any workable sorbent cartridge. Further, the ZrP layer of the REDY cartridge would be replaced by the MGP of Polak et al. as explained above; therefore, the REDY cartridge would not have a cation exchange layer, as the ZrP layer was replaced by MGP. Certainly, Polak et al. does not teach or suggest that the mixture of materials in Polak et al. can be used with other sorbent materials in a layer form. Further, the REDY cartridge does not teach or suggest that any one layer can be substituted with a different chemical substance.

Accordingly, for the reasons set forth above, even if somehow the REDY cartridge could be combined with Polak et al., one skilled in the art would still not consider claims 32-36 of the present application as obvious. Accordingly, the rejection of these claims should be reversed.

B. The Examiner's rejection of claim 2 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Smakman et al. (U.S. Patent No. 4,542,015).

1. The Examiner's rejection.

At page 7 of the Office Action dated August 20, 2004, the Examiner rejects claim 2 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Smakman et al. (U.S. Patent No. 4,542,015). The Examiner asserts that the REDY cartridge describes the use of HZO-Ac as a separate layer for PO_4 absorption. The Examiner then continues to assert that Polak et al. describes SZC as the state of the art for PO_4 absorber. Additionally, the Examiner states that Polak et al. describes that SZC is the state of the art for phosphate ion absorption because of the problems associated with HZO as taught by Smakman et al. (toxic side effect, reproducibility, and rapid deterioration). Also, according to the Examiner, SZC and HZO-Ac are equivalent and perform the identical functions specified in the

claims of Polak et al., in substantially the same way, and produce substantially the same results as the corresponding elements disclosed in the specification. Therefore, the Examiner concludes that the REDY cartridge in view of Polak et al. and further in view of Smakman et al. teaches the claimed invention.

For the following reasons, this rejection is respectfully reversed.

2. The Appellant's reply to the Examiner's rejection of claim 2 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Smakman et al. (U.S. Patent No. 4,542,015).

a) The patentability of claim 2.

In terms of the claim at issue, the following summary is provided:

Claim 2 is dependent on claim 1 and recites that the sodium zirconium carbonate is present as a layer in the sorbent cartridge wherein one of the layers consists essentially of sodium zirconium carbonate.

The language "consisting essentially of" is an introductory term used in patent claims, which commonly follows the preamble of a claim and introduces the elements making up the claim. The use of the term "consisting essentially of" to introduce the elements of a claim leaves the claim open only for the inclusion of other components, ingredients, or process steps that do not materially affect the basic and novel characteristics of the invention.

As stated above, claim 2 recites that one of the layers consists essentially of SZC, which means that one of the layers includes SZC and other components or ingredients that do not materially affect the basic and novel characteristics of the layer.

As stated above, Polak et al. does not teach or suggest that the SZC is present as a layer in a sorbent cartridge. SZC is never used alone in Polak et al. Polak et al. requires that SZC be used with

MGP. *See* Figure 2 and column 6, lines 9-11. Polak et al. only describes a mixture of MGP and SZC components in a pouch. Given that MGP is a critical and the primary ingredient of Polak et al., Polak et al. does not teach or suggest a layer that consists essentially of sodium zirconium carbonate.

The REDY cartridge includes layers; however, none of the layers in the REDY cartridge includes an SZC layer. Furthermore, there is no teaching, suggestion, or motivation to separate the mixture of the MGP and SZC, in order to form SZC alone into a layer, and then to replace one of the layers of the REDY cartridge with the formed SZC layer.

Smakman et al. relates to an apparatus for purifying blood, which includes a blood compartment and a clearance compartment separated by a semi-permeable membrane. Smakman et al. does not at all relate to SZC and does not teach or suggest any substitution to replace a layer with SZC. The Examiner's reliance on this reference is not understood. The Examiner asserts that this Smakman et al. reference justifies the obviousness of claim 2 which recites a layer consisting essentially of sodium zirconium carbonate. As stated, Smakman et al. does not show a sorbent cartridge having two layers where one layer consists essentially of sodium zirconium carbonate and certainly Polak et al. does not teach or suggest a sorbent cartridge having two layers where one layer consists essentially of sodium zirconium carbonate. As stated, Polak et al. clearly shows a pouch or capsule of MGP with SZC. Further, as stated, the REDY cartridge does not show a sodium zirconium carbonate layer. Thus, not a single reference relied upon by the Examiner shows a layer consisting essentially of sodium zirconium carbonate. Thus, even if all of the references are combinable, one still does not have a sorbent cartridge having two layers where one layer consists essentially of sodium zirconium carbonate. The Examiner clearly has not meet his burden of a *prima facie* case of obviousness.

The apparatus of Smakman et al. includes a device containing a cation exchange resin charged with metal ions whose phosphates are insoluble in water. Smakman et al., at column 2, lines 31-37, indicates that several disadvantages are associated with the use of inorganic ion exchangers for removing phosphates from the dialysis liquid. According to Smakman et al., hydrated or non-hydrated aluminum oxide, for instance, displays a toxic side effect; a satisfactorily reproducible preparation of hydrated zirconium oxide is found to give several problems; and the phosphate-retaining capacity of hydrated iron oxide rapidly deteriorates with time.

Contrary to the Examiner's assertions at page 8 of the Office Action dated August 20, 2004, Smakman et al. does not teach that hydrous zirconium oxide has toxic side effects and problems with rapid deterioration. Column 2, lines 31-37 of Smakman et al., clearly states that the problems with respect to toxic side effect are with reference to non-hydrated aluminum oxide and the effects of rapid deterioration are with respect to hydrated iron oxide. Accordingly, the Examiner is misreading Smakman et al. Moreover, Smakman et al. does not teach or suggest replacing the hydrated zirconium oxide with sodium zirconium carbonate. Furthermore, as emphasized above, there is no teaching, suggestion, or motivation to separate the mixture of the MGP and SZC of Polak et al. in order to form SZC alone into a layer, and then to replace one of the layers of the REDY cartridge with the formed SZC layer.

With respect to the Examiner's argument at page 8 of the Office Action dated August 20, 2004, that SZC and HZO-Ac are equivalent and perform the identical functions specified in the claim in substantially the same way and produces substantially the same results as the corresponding element disclosed in the specification, and with respect to the Examiner's reliance on *Kemco Sales, Inc. v. Control Papers Co.,* 54 U.S.P.Q.2d 1308 (Fed. Cir. 2000), the Appellant responds as follows. First of all, the standard referred to by the Examiner is not the standard

under § 103. Second, the legal decision relied upon by the Examiner has nothing to do with the patentability of the claims under § 102 or § 103. The Appellants do not understand how the Examiner can rely on this legal decision to support this rejection and it appears that the Examiner is applying a Doctrine of Equivalents infringement standard when the issue involved in the present application is the patentability of the claims. It appears the Examiner is in clear error.

In addition, the *Kemco Sales* decision relates to means plus function claim language which does not exist in claim 2. Clearly, the *Kemco Sales* legal decision is irrelevant to the issues on appeal.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system, Polak et al. relates to an encapsulated capsule for oral consumption. See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the two references would not be combinable for this reason as well.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al., and further in view of Smakman et al. does not render the claimed invention unpatentable and the rejection of claim 2 should be reversed.

C. The Examiner's rejection of claims 26-28 under 35 U.S.C. § 103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Potts (U.S. Patent No. 5,234,603).

1. The Examiner's rejection.

At page 8 of the Office Action dated August 20, 2004, the Examiner rejects claims 26-28 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and

further in view of Potts (U.S. Patent No. 5,234,603). The Examiner asserts that the REDY cartridge includes ZrO for purifying spent dialysate. Furthermore, the Examiner states that Potts describes a basic zirconium carbonate for removal of heavy metals, transition metals, and organic matter from wastewater, and that zirconium carbonate would hydrolyze to form a polymeric oxide chain. Thus, the Examiner concludes that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to have the teachings of the REDY cartridge and Potts in the teaching of Polak et al. for purifying the spent dialysate as taught by Polak et al. In addition, the Examiner states that Potts, at col. 4, line 35, describes that the zirconium carbonate would hydrolyze to form a polymeric oxide chain.

For the following reasons, the Examiner's rejection should be reversed.

2. The appellant's reply to the Examiner's rejection of claims 26-28 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Potts (U.S. Patent No. 5,234,603).

a) The patentability of claims 26-28.

In terms of the claims at issue, the following summary is provided:

Claim 26 is dependent on claim 1 and recites that the sorbent cartridge further comprises zirconium basic carbonate.

Claim 27 is dependent on claim 26 and recites that the zirconium basic carbonate includes Na^+ of less than about 1000 ppm; a ZrO_2 wt% of from about 35 wt% to about 40 wt%; and a CO_3^{2-} of from about 8 wt% to about 10 wt%, based on the weight of the zirconium basic carbonate.

Claim 28 is dependent on claim 27 and recites that the zirconium basic carbonate has about 0 wt% SO_4^{2-} and about 0 wt% Cl^-.

The arguments set forth above with respect to the REDY cartridge and Polak et al. apply equally here.

Further, Polak et al. relates to the preparation of MGP and its use in the medical field, its use in recirculating dialysis systems and other systems having the purpose of removing urea/ammonia from bodily fluids, and in wastewater treatment to remove ammonium ions. In contrast, according to Potts, at column 3, lines 55-61, the contaminants to be removed include actinide and lanthanide metals, transition metals, heavy metals, suspended solids (either organic, inorganic, and/or biological), alkaline earth metals, and similar insoluble materials (and materials which can be made insoluble) in the wastewater. Potts does not teach or suggest removal of urea or ammonia.

Furthermore, the zirconium carbonate in Potts is not used as an ion-exchange material to remove the contaminants from wastewater. In fact, a reading of Potts indicates that its zirconium carbonate is used as a precipitating agent by itself or in combination with a coagulating agent, a reducing agent, or a weighting agent. Thus, the zirconium carbonate of Potts must be a soluble salt. Therefore, given that the zirconium carbonate of Potts is a soluble salt, it cannot form a layer in a sorbent cartridge. The two references are simply not within the same field of endeavor. Accordingly, one skilled in the art seeking to learn about the removal of urea/ammonia from bodily fluids would not look to Potts. The Examiner cannot use hindsight to mix and match the layers. Absolutely no suggestion is made in either reference for mixing and matching the layers.

In addition, Polak et al. is not combinable with REDY because the REDY cartridge disclosure as shown in the "Guide to Custom Dialysis" and "Sorbent Dialysis Primer," both of which are attached, clearly relates to a cartridge system which is outside of the patient. Unlike the REDY system and Potts, Polak et al. relates to an encapsulated capsule for oral consumption.

See, for instance, column 1, lines 19-22; column 3, lines 30-36; column 5, lines 26-31; and the claims of Polak et al. Thus, the references would not be combinable for this reason as well.

Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al. and Potts does not render the claimed invention unpatentable, and the rejection of claims 26-28 should be reversed.

D. The Examiner's rejection of claims 17 and 18 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Marantz et al. (U.S. Patent No. 3,669,880).

1. The Examiner's rejection.

At page 9 of the Office Action dated August 20, 2004, the Examiner rejects claims 17 and 18 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Marantz et al. (U.S. Patent No. 3,669,880). According to the Examiner, claims 17 and 18 of the present application add structural components like filter pads and a diffuser. The Examiner then states that the REDY cartridge includes a filter pad (Fig. 1), but not the diffuser for flow distribution. However, the Examiner states that Marantz et al. describes a flow distributor and filter pads. Thus, the Examiner concludes that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to use the teaching of Marantz et al. in the teaching of the REDY cartridge in view of Polak et al. for the flow distribution and for preventing the breakup and inter-mixing of particles in layers as taught by Marantz et al. The Examiner further states that Marantz et al. is used to show a flow distributor and filter pads.

For the following reasons, the Examiner's rejection should be reversed.

2. The appellant's reply to the Examiner's rejection of claims 17 and 18 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further

in view of Marantz et al. (U.S. Patent No. 3,669,880).

a) The patentability of claims 17 and 18.

In terms of the claims at issue, the following summary is provided:

Claim 17 is dependent on claim 16 and recites that the sorbent cartridge further comprises a first filter pad located above and in contact with the sodium zirconium carbonate, a second filter pad is located between and in contact with the alumina supported urease and the granular activated carbon, and a third filter pad is located beneath and in contact with the granular activated carbon.

Claim 18 is dependent on claim 17 and recites the sorbent cartridge further includes a flow diffuser located beneath and in contact with the third filter pad.

The arguments set forth above with respect to Polak et al. and the REDY cartridge apply equally here. As indicated, if Polak et al. teaches that magnesium phosphate replaces ZrP, then, when Polak et al. is combined with the REDY cartridge, there will be no ZrP layer in the REDY cartridge because it has been replaced by magnesium phosphate.

Further, Marantz et al. relates to a recirculating dialysate system for use with an artificial kidney in which the total volume of dialysate solution is controlled. According to Marantz et al., the urea in the solution is removed in a ZrP column, and the other waste products are removed in the carbon column containing activated carbon and hydrated zirconium oxide. In contrast, Polak et al. teaches away from Marantz et al. by replacing the ZrP with MGP. Thus, by reading Polak et al., one skilled in the art would conclude that as the composition of Polak et al. is different from Marantz et al., the cartridge used in Marantz et al. would not work in Polak et al. Therefore, one skilled in the art would not be motivated to combine Polak et al. and Marantz et al.

Additionally, the purpose of the flow distributor and filter pads of Marantz et al. are to prevent breakup and intermixing of particles in layers; however, Polak et al. describes a pouch

having intermixed particles of MGP and SZC. Also, as stated above, Polak et al. relates to an oral capsule which is completely different from the systems of REDY and Marantz et al. Therefore, one skilled in the art would not look to Marantz et al. that describes a flow distributor and a filter to prevent intermixing of particles.

Furthermore, Marantz et al. has an issue date of June 13, 1972 and Polak et al. has an issue date of March 17, 1987. As indicated on the face page of Polak et al., the inventors of Polak et al. were well aware of Marantz et al. However the inventors of Polak et al. did not incorporate the fluid distributor and filter pads of Marantz et al. in Polak et al. Thus, clearly one of ordinary skill in the art would not have been motivated to combine the teachings of the REDY cartridge in view of Polak et al. with the teachings of Marantz et al.

Accordingly, for the reasons stated above, Polak et al. in view of the REDY cartridge and further in view of Marantz et al. does not render the claimed invention unpatentable and the rejection of claims 17 and 18 should be reversed.

E. The Examiner's rejection of claim 10 under 35 U.S.C. §103(a) as being unpatentable over the "Applicant's own disclosure of prior art" of the REDY cartridge in view of Polak et al., and further in view of Tawil et al. (U.S. Patent No. 4,025,608).

1. The Examiner's rejection.

At page 9 of the Office Action dated August 20, 2004, the Examiner rejects claim 10 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Tawil et al. (U.S. Patent No. 4,025,608). The Examiner asserts that ZrP has an average grain size of from about 30 to about 40 microns, which Polak et al. in view of the REDY cartridge does not teach. However, the Examiner states that Tawil et al. describes the particle size of the ZrP. Thus, the Examiner concludes that it would have been obvious to one of ordinary skill

in the art, at the time the invention was made, to use the zirconium oxide particle size of Tawil et al. in the teaching of Polak et al. in view of the REDY cartridge for good flow distribution.

For the following reasons, the Examiner's rejection should be reversed.

2. The Appellant's reply to the Examiner's rejection of claim 10 under 35 U.S.C. §103(a) as being unpatentable over the REDY cartridge in view of Polak et al., and further in view of Tawil et al. (U.S. Patent No. 4,025,608).

a) The patentability of claim 10.

In terms of the claims at issue, the following summary is provided:

Claim 10 is dependent on claim 3 and recites that the zirconium phosphate has an average grain size of from about 30 to about 40 microns.

The arguments set forth above with respect to the REDY cartridge and Polak et al. apply equally here. As stated, if Polak et al. teaches that magnesium phosphate replaces ZrP, then, when Polak et al. is combined with the REDY cartridge, there will be no ZrP layer in the REDY cartridge as it has been replaced by magnesium phosphate.

Further, Tawil et al. relates to a ZrP that is made by reacting a zirconium salt with a phosphoric acid or a phosphate in a liquid medium, wherein the zirconium salt is insoluble in water. The Examiner cannot simply substitute different particles and argue that the substituted particles automatically have the same size as the original particles. No support exists for such a conclusion. According to Tawil et al., at column 2, lines 54-59, the grain size of the ZrP is at least 30 microns. As discussed above, Polak et al. even teaches away from utilizing a ZrP. Thus, by reading Polak et al., one skilled in the art would not be motivated to look to Tawil et al. for any guidance.

Furthermore, as stated earlier, one skilled in the art could not combine the teachings of Polak et al. with the REDY cartridge, and, even if combined, a mixture of various components, and

not layers, would be used. Also, Polak et al. replaces ZrP with magnesium phosphate; therefore, if Polak et al. is combined with the REDY cartridge, no ZrP layer would exist, as the ZrP of the REDY cartridge is replaced by the magnesium phosphate of Polak et al. The Examiner cannot have it both ways. Therefore, one skilled in the art would not be motivated to combine the REDY cartridge with Polak et al. and Tawil et al. to derive claim 10 of the present application.

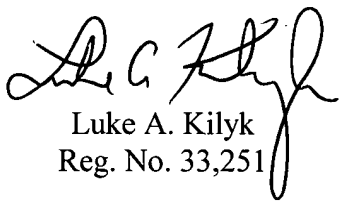
Accordingly, for the reasons stated above, the REDY cartridge in view of Polak et al., and further in view of Tawil et al. does not render the claimed invention unpatentable and the rejection of claim 10 should be reversed.

CONCLUSION

For at least the reasons discussed above, it is respectfully submitted that the Examiner's rejection of all the pending claims is in error and should be reversed.

If there is any fee due in connection with the filing of this Brief on Appeal, please charge the fee to our Deposit Account No. 50-0925.

Respectfully submitted,



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CLAIMS APPENDIX

1. A sorbent cartridge comprising at least two layers, wherein one of said layers comprises at least sodium zirconium carbonate in said sorbent cartridge.

2. The sorbent cartridge of claim 1, wherein one of said layers consists essentially of sodium zirconium carbonate.

3. The sorbent cartridge of claim 1, further comprising zirconium phosphate.

4. The sorbent cartridge of claim 3, wherein said zirconium phosphate is present as a layer in said sorbent cartridge.

5. The sorbent cartridge of claim 3, wherein said zirconium phosphate comprises a H^+ content of from about 1.4 to about 2.0 wt%;

a Na^+ content of from about 4 to about 6 wt%;

a ZrO_2 wt% of from about 34 wt% to about 37 wt%;

a PO_4 wt% of from about 41 wt% to about 43 wt%; and

a H_2O wt% of from about 14 wt% to about 18 wt%, based on the weight of the zirconium phosphate.

6. The sorbent cartridge of claim 3, wherein said zirconium phosphate has at least one of the following characteristics:

a) an adsorption capacity for ammonia of from about 20 mg NH_4-N/gm ZrP to about 45 mg NH_4-N/gm ZrP;

an adsorption capacity for Ca^{2+} of from about 2 mEq Ca^{2+}/gm ZrP to about 7 mEq Ca^{2+}/gm ZrP;

an adsorption capacity for Mg^{2+} of from about 1 mEq Mg^{2+}/gm ZrP to about 5 mEq Mg^{2+}/gm ZrP; and

an adsorption capacity for toxic heavy metals of from about 3 mEq HM/gm ZrP to about 9 mEq HM/gm ZrP;

b) a Na^+ content of from about 1.8 mEq Na^+/gm ZrP to about 3 mEq Na^+/gm ZrP at a pH of from about 5.5 to about 6;

c) a minimum leachable PO_4^{3-} of less than about 0.05 mg PO_4^{3-}/gm ZrP; or

d) satisfying ANSI/AAMI RD-5-1992 standard on extractable toxic impurities.

7. The sorbent cartridge of claim 5, wherein said zirconium phosphate has no residual sulfate or chloride.

8. The sorbent cartridge of claim 5, wherein said zirconium phosphate has less than 0.01% sulfate, chloride, or both.

9. The sorbent cartridge of claim 3, wherein said zirconium phosphate in H_2O has a pH of from about 6 to about 7.

10. The sorbent cartridge of claim 3, wherein said zirconium phosphate has an average grain size of from about 30 to about 40 microns.

11. A sorbent cartridge comprising an alkali metal-Group IV B metal carbonate, wherein said alkali metal-Group IV B metal carbonate is present as a layer in said sorbent cartridge.

13. The sorbent cartridge of claim 11, further comprising a Group IV B metal phosphate.

14. The sorbent cartridge of claim 1, further comprising alumina, alumina supported urease, granular activated carbon, or combinations thereof.

15. The sorbent cartridge of claim 14, wherein said alumina, alumina supported urease, and granular activated carbon are each present as separate layers in said sorbent

cartridge.

16. The sorbent cartridge of claim 15, wherein said layers have the following order:

a) said sodium zirconium carbonate;

b) a zirconium phosphate;

c) said alumina;

d) said alumina supported urease;

e) said granular activated carbon.

17. The sorbent cartridge of claim 16, wherein said sorbent cartridge further comprises a first filter pad located above and in contact with said sodium zirconium carbonate, a second filter pad is located between and in contact with said alumina supported urease and said granular activated carbon, and a third filter pad is located beneath and in contact with said granular activated carbon.

18. The sorbent cartridge of claim 17, further comprising a flow diffuser located beneath and in contact with said third filter pad.

19. The sorbent cartridge of claim 1, wherein said sodium zirconium carbonate comprises from about 2 wt% to about 5 wt% Na^+;

from about 44 wt% to about 50 wt% ZrO_2;

from about 12 wt% to about 18 wt% CO_3^{2-}; and

from about 30 wt% to about 40 wt% LOD, based on the weight of the sodium zirconium carbonate.

20. The sodium zirconium carbonate of claim 1, wherein said sodium zirconium carbonate satisfies ANSI/AAMI RD-5-1992 standard on extractable toxic impurities.

21. The sodium zirconium carbonate of claim 1, wherein said sodium zirconium

carbonate satisfies at least one of the following characteristics:

a phosphate adsorption having a minimum capacity of from about 30 to about 35 mg/PO_4-P/gm SZC;

a minimum HCO_3^- content of from about 2 to about 4 mEq HCO_3^- per gm SZC;

a leachable Na^+ content of from about 1.5 to about 2.0 mEq Na^+/gm SZC;

or a pH range of titrated sodium zirconium carbonate of from about 6 to about 7.

22. The sorbent cartridge of claim 1, further comprising hydrous zirconium oxide.

23. The sorbent cartridge of claim 22, wherein said hydrous zirconium oxide is in the acetate form.

24. The sorbent cartridge of claim 23, wherein said sodium zirconium carbonate and said hydrous zirconium oxide are present in a weight ratio of about 1 to 1.

25. The sorbent cartridge of claim 23, wherein said sodium zirconium carbonate and said hydrous zirconium oxide are present in a same layer and are blended together.

26. The sorbent cartridge of claim 1, further comprising zirconium basic carbonate.

27. The sorbent cartridge of claim 26, wherein said zirconium basic carbonate comprises Na^+ of less than about 1000 ppm;

a ZrO_2 wt% of from about 35 wt% to about 40 wt%;

and a CO_3^{2-} of from about 8 wt% to about 10 wt%, based on the weight of the zirconium basic carbonate.

28. The sorbent cartridge of claim 27, wherein said zirconium basic carbonate has about 0 wt% SO_4^{2-} and about 0 wt% Cl^-.

29. The sorbent cartridge of claim 1, wherein said sodium zirconium carbonate is present in said cartridge in an amount of from about 100 grams to about 300 grams.

30. The sorbent cartridge of claim 29, wherein said cartridge further comprises zirconium phosphate in an amount of from about 300 grams to about 1900 grams.

31. The sorbent cartridge of claim 30, further comprising alumina in the amount of from about 100 grams to about 500 grams, immobilized enzyme in an amount of from about 100 grams to about 300 grams, and activated carbon or other adsorbent in an amount of from about 100 grams to about 500 grams.

32. The sorbent cartridge of claim 1, further comprising an immobilized enzyme material capable of enzymatic conversion of urea to ammonium carbonate, a cation exchange material in the sodium or hydrogen form, an anion exchange material in the Ac^-, HCO_3^-, Cl^-, or OH^- form, and an adsorbent capable of removing creatinine, uric acid, or both.

33. The sorbent cartridge of claim 32, further comprising a chlorine removal material.

34. The sorbent cartridge of claim 32, wherein the materials are present as two or more layers in said cartridge.

35. The sorbent cartridge of claim 33, wherein the materials are present as two or more layers in said cartridge.

36. The sorbent cartridge of claim 11, further comprising an immobilized enzyme material capable of enzymatic conversion of urea to ammonium carbonate, a cation exchange material in the sodium or hydrogen form, an anion exchange material in the Ac^-, HCO_3^-, Cl^-, or OH^- form, and an adsorbent capable of removing creatinine, uric acid, or

both.

37. The sorbent cartridge of claim 11, further comprising a chlorine removal material.

38. The sorbent cartridge of claim 11, wherein the materials are present as two or more layers in said cartridge.

40. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 1.

42. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 3.

43. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 4.

44. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 5.

45. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 6.

46. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 11.

48. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 13.

49. A method to regenerate or purify spent dialysis fluid comprising passing said spent dialysis fluid through the sorbent cartridge of claim 16.

50. An apparatus for conducting dialysis comprising the sorbent cartridge of claim 1, a dialyzer in fluid communication with said cartridge wherein spent dialysis fluid passes

from said dialyzer to and through said cartridge.

51. The apparatus of claim 50, wherein said spent dialysis fluid is spent hemodialysis fluid.

52. The apparatus of claim 50, wherein spent dialysis fluid is restored to original balance of Na^+ and HCO_3^- contents found in fresh dialysate.

53. The apparatus of claim 50, wherein said dialyzer is in fluid communication with the blood of a patient.

54. The apparatus of claim 53, wherein the Na^+ and HCO_3^- balance in said blood is restored to levels found in healthy patient without renal problems.

55. The apparatus of claim 50, wherein said spent dialysis fluid is spent dialysate fluid obtained from a dialyzer wherein spent peritoneal dialysis fluid is passed through said dialyzer and cleaned by fresh dialysate fluid.

56. A dialysis system comprising the sorbent cartridge of claim 1 and a source of spent peritoneal dialysis solution, wherein the source of said spent peritoneal dialysis solution is in fluid communication with said cartridge wherein said spent peritoneal dialysis solution passes to and through said cartridge.

57. The sorbent cartridge of claim 1, wherein said cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in fresh dialysate.

58. The sorbent cartridge of claim 5, wherein said cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in fresh dialysate.

59. The sorbent cartridge of claim 31, wherein said cartridge is capable of restoring the balance of Na^+ and HCO_3^- in spent dialysate to levels found in fresh dialysate.

60. The sorbent cartridge of claim 3, wherein said zirconium phosphate is further

away from an inlet opening of said sorbent cartridge than said layer of sodium zirconium carbonate.

61. The sorbent cartridge of claim 4, wherein said layer of zirconium phosphate is further away from an inlet opening of said sorbent cartridge than said layer of sodium zirconium carbonate.

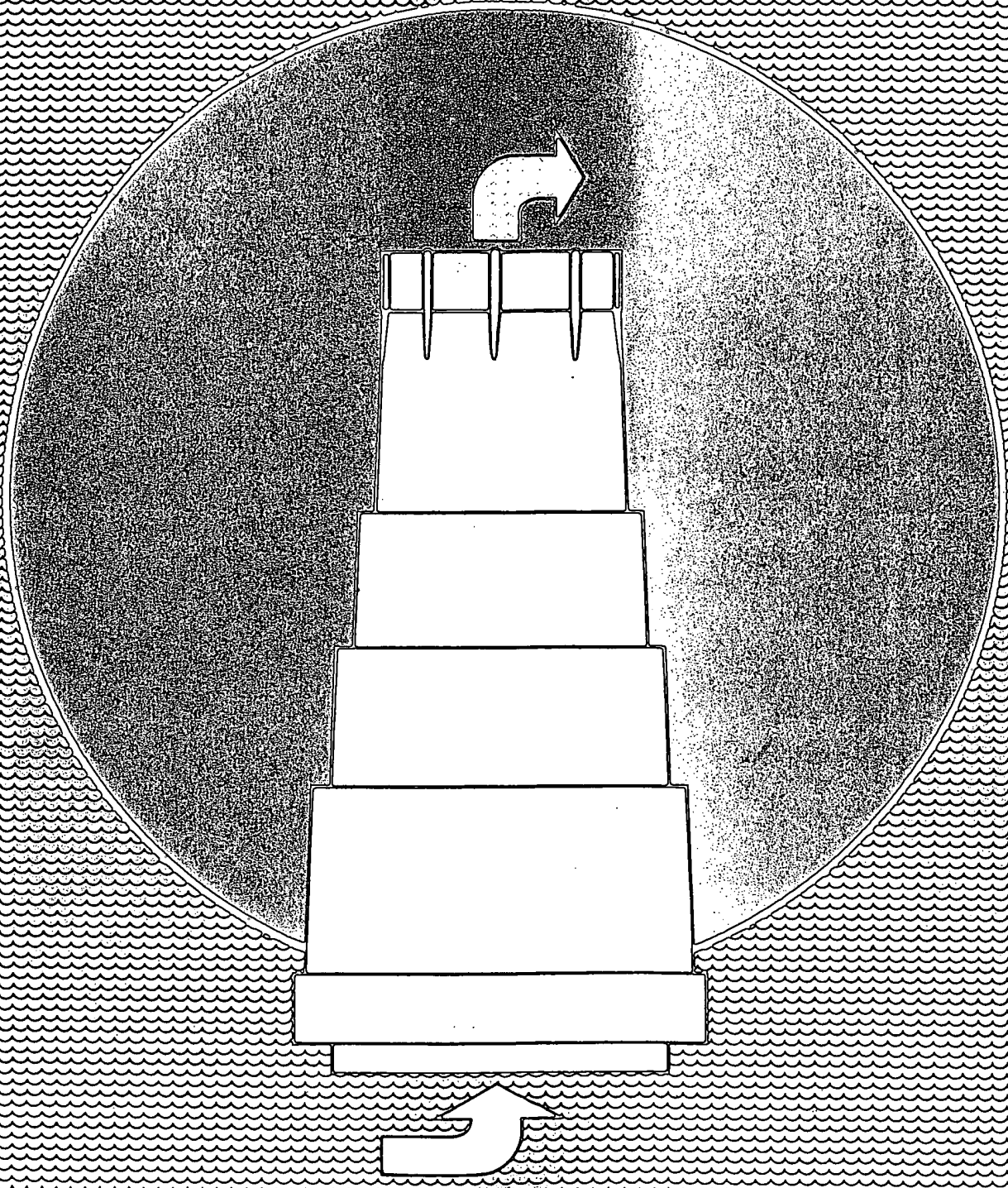
EVIDENCE APPENDIX

No evidence that has been entered by the Examiner is relied upon by the appellant.

RELATED PROCEEDINGS APPENDIX

No related proceedings that would directly affect or be directly affected by or have a bearing on the Board's decision in this appeal is known to the appellant or the appellant's legal representative.

Sorbent Dialysis Primer



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FOREWORD

THIS IS NOT AN OPERATOR'S MANUAL FOR SORBENT DIALYSIS EQUIPMENT.

The **Sorbent Dialysis Primer** has been prepared for use by clinical personnel who are knowledgeable about the principles of hemodialysis but are not completely familiar with the principles of sorbent dialysis. The Primer contains an explanation of these basic principles and some techniques for applying them to clinical situations.

Since the focus of the Primer is on mastering the fundamentals of sorbent dialysis, the techniques discussed in the Primer are centered primarily on dialysis of relatively stable patients. Information about customized dialysates and procedures for unstable acutes, drug overdose patients and special ultrafiltration procedures can be found in the Guide to Custom Dialysis, also available from COBE Renal Care.

The term SUN (Serum Urea Nitrogen) is used throughout this book for reasons of technical accuracy; most laboratories measure the urea nitrogen level of serum rather than whole blood.

If questions arise regarding the contents of the Primer, please contact COBE Renal Care. Your REDY sales consultant has been trained in the principles and operation of REDY Sorbent Dialysis Systems. He or she will provide your initial inservice and will be glad to answer questions then or at any time in the future.

The Customer Information Center staff is available 24 hours a day to answer questions by telephone. Simply dial 1-800-456-7339 and ask to speak with a dialysis nurse.

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COMPONENTS OF SORBENT DIALYSIS

1.1. INTRODUCTION TO SORBENT DIALYSIS

Sorbent dialysis differs from single pass dialysis in one major respect: used dialysate is chemically reprocessed into fresh new dialysate and sent back to the dialyzer instead of being sent down the drain. REDY Sorbent Dialysis Systems use a column of special chemicals—the Sorbent Cartridge—to regenerate used dialysate.

REDY Sorbent Dialysis Systems (Figure 1.1) incorporate two basic components: (1) a 6 liter reservoir for storing fresh dialysate, and (2) a Sorbent Cartridge and infusate system, which together reprocess used dialysate into fresh dialysate.

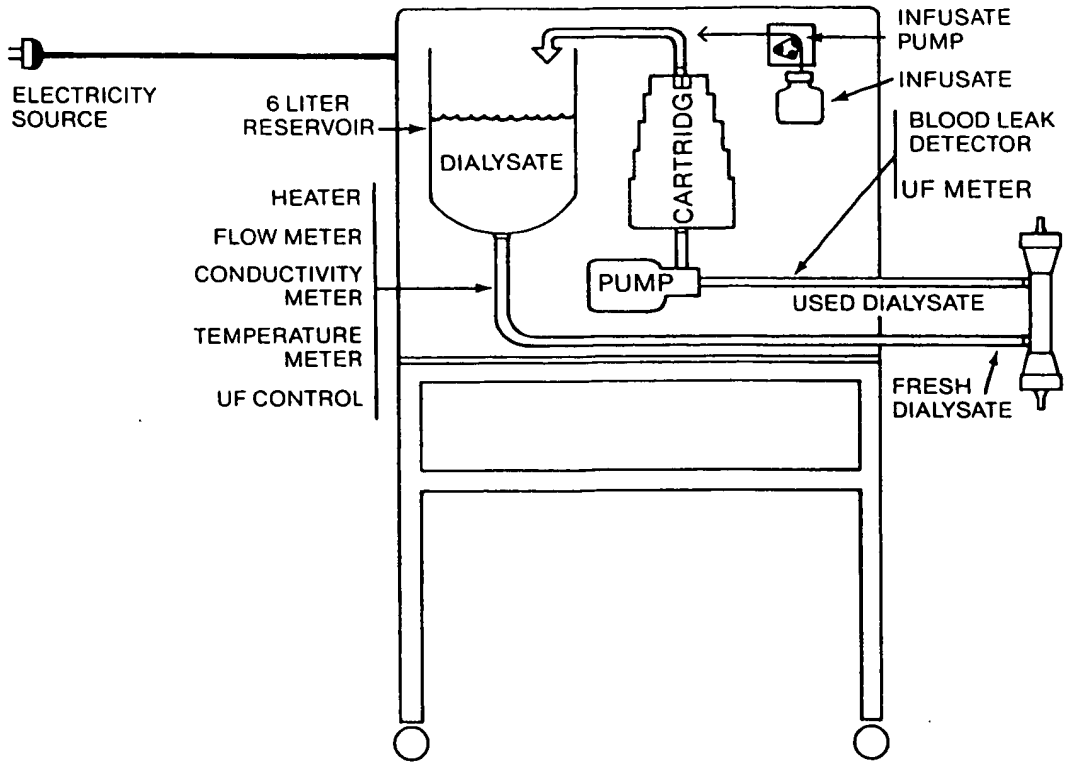


Figure 1.1: REDY Sorbent Dialysis System

Other than the method by which fresh dialysate is produced, REDY Sorbent Dialysis Systems are like single pass dialysis machines. Both dialysis systems provide warm dialysate, monitored for proper temperature and conductivity, to the dialyzer as well as apply measured amounts of negative pressure and detect blood in dialysate leaving the dialyzer.

However, that one difference—regeneration of used dialysate—leads to a number of advantages over contemporary single pass dialysis systems.

A. **Only a small amount of dialysate is necessary to perform dialysis.** REDY Sorbent Dialysis Systems use only 6 liters of dialysate. This results in conservation of increasingly costly resources: the electricity used to pump and heat large volumes of dialysate as well as the purified water and chemicals used to prepare it.

B. **It is easy to alter the composition of the dialysate.** The unique properties of the Sorbent Cartridge and infusate system (explained in Sections 2 and 3 of this Chapter), together with the small volume of dialysate used (6 liters), make it easy and inexpensive to provide an infinite variety of both acetate and bicarbonate dialysates in response to the needs of individual patients. No additional equipment, such as a bicarbonate or sodium control module, is required. Various bath compositions are achieved by adding the contents of small packets of dry chemicals to the system. Thus, the space required to store a large inventory of different dialysate concentrates is reduced to approximately two cubic feet.

C. **The regenerated dialysate is recirculated.** Since used dialysate is regenerated and sent back to the dialyzer instead of being discarded, it is not necessary to have a floor drain or to continuously provide water and concentrate to the machine during dialysis. As a result, there are no hoses on the

1.1 INTRODUCTION TO SORBENT DIALYSIS (continued)

floor to leak water or trip over. During dialysis REDY Sorbent Dialysis Systems require only electricity. This means Sorbent Dialysis can be performed anywhere: in dialysis centers, critical care units, hospital rooms, even hotel rooms, campers and aboard ships during ocean cruises.

D. **The dialysate pathway is a closed system**. Nothing goes down the drain. Not even ultrafiltrate. Ultrafiltrate removed from the patient enters the Sorbent Cartridge, is converted into dialysate and carried to the reservoir with the regenerated dialysate. Thus any increase in the volume of dialysate in the reservoir is due to the accumulation of ultrafiltrate (unless the operator deliberately adds fluid to the reservoir. There are reasons this may be done. See Section 2.3.C., p. 19). The volume of fluid in the reservoir is continuously displayed. This provides a direct measurement of ultrafiltration, not an estimate. As a result, the patient's fluid status is always known and treatment parameters can be altered as necessary to achieve exact ultrafiltration goals.

E. **The Sorbent Cartridge is a water treatment system**. Since the Cartridge can remove bacteria, pyrogen, and undesirable chemicals from dialysate made from most tap water, it is rarely necessary to use treated water with REDY Sorbent Dialysis Systems. This not only frees the owner of the need to purchase and maintain an expensive water treatment system but provides a dialysis machine with an unusual degree of portability.

F. **Home hemodialysis patients have an exceptional amount of freedom**. The machine need not be confined to a particular "dialysis room" in the home so each treatment can be performed wherever the patient wishes to be, even the patio or back yard. No room is avoided by the family because it reminds them of dialysis, thereby effectively reducing available living space. Household utility bills will not show a significant increase in water and electricity costs. Vacations can be taken anywhere, any time.

In summary, REDY Sorbent Dialysis Systems provide the operator with an unusual degree of portability, treatment flexibility and ultrafiltration control while freeing the dialysis center of various expenses such as high utility bills, water treatment equipment, special sodium and bicarbonate proportioning systems and extensive storage space.

It should be apparent by now that such a unique system requires a knowledge of principles that are different, although not necessarily more difficult, than those required to perform single pass dialysis. The rest of this booklet provides the information necessary to perform Sorbent Dialysis.

Additional resources are available, as well. Your COBE Renal Care Sales Consultant has been trained in the principles and operation of REDY Sorbent Dialysis Systems, and will provide your initial inservice. COBE also maintains a Customer Information Center staffed by nurses experienced in hemodialysis, who are available to answer questions by telephone. Simply dial our toll-free number, 800-456-7339, and ask to speak with a dialysis nurse.

1.2 THE SORBENT CARTRIDGE

1.2.A Basic Principles

Sorbent dialysis systems work because they take advantage of some basic principles of chemistry. These principles are:

FIRST: Activated carbon binds a large variety of substances and will not release them. For that reason activated carbon is used as a universal antidote for poisoning and is the major component in hemoperfusion devices used to treat severe drug overdose.

SECOND: An enzyme named urease breaks urea into ammonium and carbonate ions. Enzymes make the biochemical reactions of metabolism possible; without them, life as we know it could not exist. For example, without urease, a person would need a body temperature of 140°C to split urea into ammonium and carbonate ions.

THIRD: Certain resins adsorb (or remove from solution) given ions in exchange for other ions. Thus a resin can be designed to take calcium out of a solution and put sodium into the solution in its place. This is how water softeners work.

The Sorbent Cartridge is designed to use these three simple principles to perform two functions. Before dialysis begins, the Cartridge removes impurities from dialysate made with tap water, thus, in most cases, eliminating the need to treat the water used to make dialysate. And once dialysis begins, the Cartridge – together with the infusate system – converts used dialysate into fresh new dialysate.

Used dialysate contains uremic toxins, most of them nitrogenous wastes such as urea, creatinine, uric acid, etc. Also, the electrolyte content of dialysate is changed as it passes through the dialyzer. Used dialysate normally contains excess potassium and phosphate ions removed from the patient's blood, while calcium and magnesium ions may have left the dialysate to enter the patient.

1.2.B. Function of Specific Layers

The Sorbent Cartridge contains five separate layers. Used dialysate enters at the bottom of the Cartridge and is purified as it rises through each succeeding layer. Cartridge effluent, the fluid which exits the top of the Cartridge, is then mixed with a carefully proportioned volume of infusate. The result is freshly regenerated dialysate. The function of each Cartridge layer is described on the following pages. Since the used dialysate enters at the bottom of the Cartridge, the description will begin with the bottom layer.

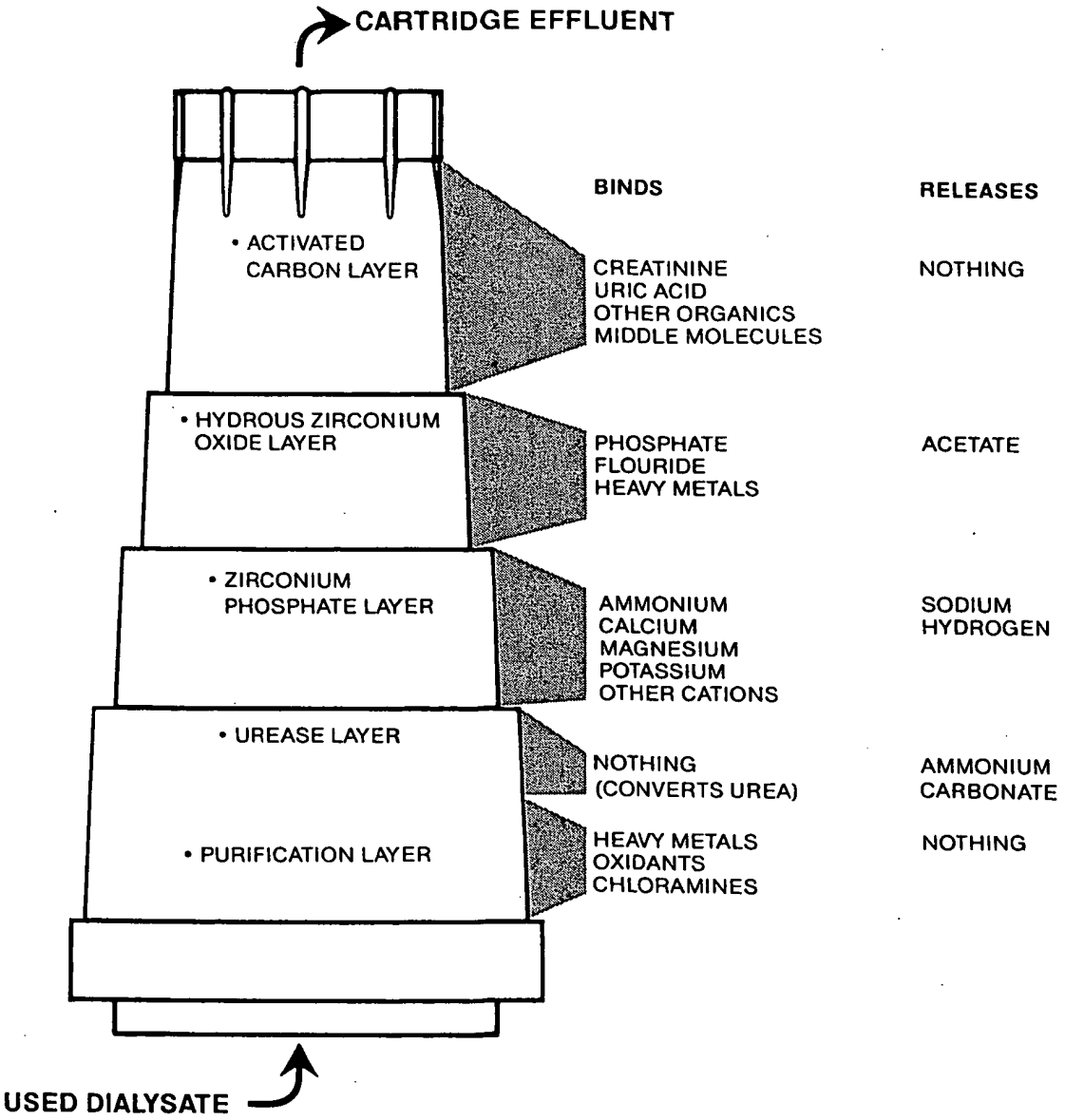


Figure 1.2: Sorbent Cartridge

Purification Layer

The first layer consists of activated carbon. This layer removes particulate matter, heavy metals (e.g., copper, mercury, lead) and oxidizing substances such as sodium hypochlorite. These substances may be present in the water used to prepare the dialysate or as trace contaminants from cleaning the machine. The purification layer will also remove small amounts of chloramines. For a complete discussion of the use of Sorbent Cartridges to purify dialysates made with tap water, see Chapter 3: Dialysate Purification.

Urease Layer

Urease is an enzyme which specifically converts urea to ammonium carbonate by several reaction steps. The ammonium and carbonate ions are carried up to the next layer.

1.2.B. Function of Specific Layers (continued)

Zirconium Phosphate Layer
Zirconium phosphate is used in the Cartridge as a cation exchanger in the sodium and hydrogen form. Cations (ions with a positive charge) such as ammonium are adsorbed (bound) by the zirconium phosphate. Calcium, potassium and magnesium, which are also cations, are adsorbed by zirconium phosphate as well. In exchange for adsorbing these cations, zirconium phosphate releases two other cations: sodium and hydrogen. Zirconium phosphate is also the salt of a weak acid and thus has the properties of a buffer. Because of its properties as both a cation exchanger and buffer, the relative amounts of sodium and hydrogen released depends on the pH and anions (acetate or bicarbonate) present in the used dialysate.

Hydrous Zirconium Oxide Layer
Hydrous zirconium oxide acts as an anion exchanger. The zirconium oxide layer in the Cartridge is in the acetate form. Thus it binds ions with a negative charge, such as phosphate and flouride, and releases acetate in exchange. Hydrous zirconium oxide is also an excellent adsorbent for metals,such as iron, mercury, lead and aluminum. It will remove these substances if they are present in the tap water used to make the initial dialysate or enter the used dialysate from the patient.

Activated Carbon Layer
The activated carbon in the Cartridge adsorbs organic metabolites such as creatinine, uric acid, and "middle molecules". Activated carbon is a "Pure Sorbent", that is, it will bind these substances without releasing anything in exchange.

1.2.C. Composition of Cartridge Effluent

The composition of the used dialysate is changed as it moves up through the layers of the Cartridge. Many substances are removed, some are added. Others pass through the Cartridge unchanged, such as water, sodium chloride and sodium acetate.

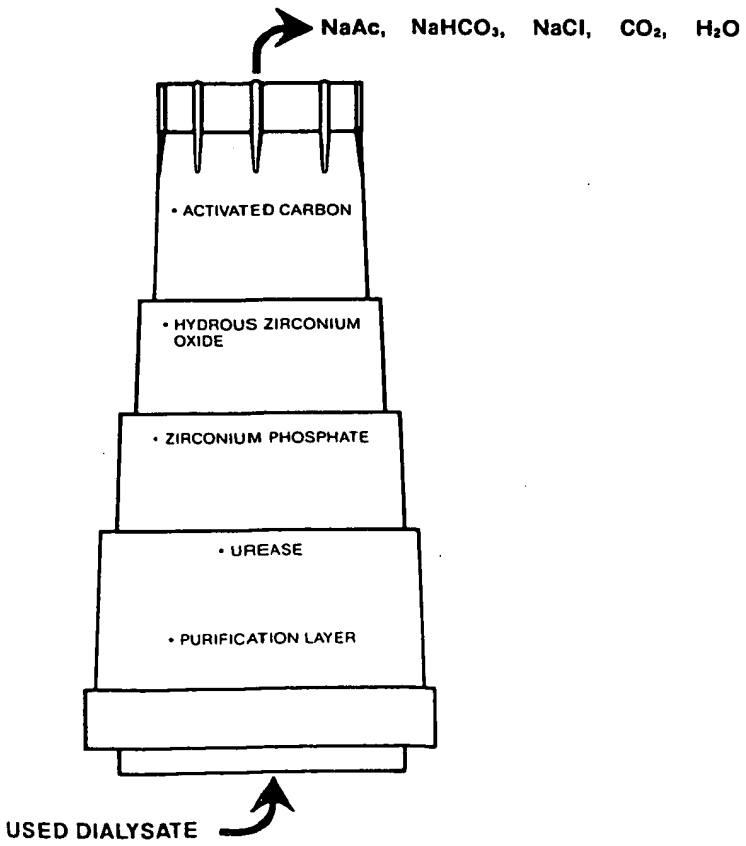


Figure 1.3: Composition of Cartridge Effluent

1.2.C. Composition of Cartridge Effluent (continued)

The Cartridge effluent is composed of those substances which pass through the Cartridge unchanged and those which are emitted by the zirconium and urease layers. For example, urease converts urea into ammonium carbonate, some of which is then converted into sodium bicarbonate in the zirconium phosphate layer. The amount of sodium bicarbonate formed depends on the amount of urea available to the Cartridge. If, by chance, the patient is not uremic, very little sodium bicarbonate will be formed.

The hydrogen ions emitted in the zirconium phosphate layer also combine with carbonate ions, forming bicarbonate (HCO_3) and carbonic acid (H_2CO_3). Carbonic acid is an unstable organic acid; most of it quickly breaks down into water and carbon dioxide molecules. This is the same thing that happens to carbonic acid when it is produced in the human body during the normal process of metabolism. The volume of water produced in the Cartridge, by the way, is negligible compared to the volume of ultrafiltrate removed from the patient. It amounts to less than 20 ml during an entire dialysis.

1.2.D Cartridge Capacity

Two types of Sorbent Cartridges are available.

1. The SORB Cartridge has an average urea-nitrogen capacity of approximately 20 grams. This Cartridge can bind the ammonia produced by the breakdown of about 20 grams of urea-nitrogen present in used dialysate. This is generally more urea than crosses the dialyzer membrane during a standard 4 hour dialysis performed on an adult chronic dialysis patient.

2. The HiSORB Cartridge has a urea-nitrogen capacity of approximately 30 grams. The HiSORB Cartridge is used for patients with high serum urea nitrogen (SUN) levels, such as acutes or large chronic dialysis patients (SUN greater than 100 mg/dl and/or body weight above 80 kg).

The only difference between the SORB and HiSORB Cartridge is their urea-nitrogen binding capacity. They are the same in all other respects, such as drug binding capacity. For additional information about the use of Sorbent dialysis in drug poisoning, see the **Guide to Custom Dialysis**, available from COBE Renal Care.

Keep in mind that the function of both sorbent cartridges is to convert and/or bind uremic toxins. Clearance of uremic toxins from the blood is still accomplished in the same manner as with single pass systems. Clearance is dependent on: (1) blood flow rate, (2) dialysate flow rate, (3) membrane characteristics, (4) membrane surface area and, (5) length of treatment. Sorbent cartridges remove from dialysate only those substances cleared from the blood by the dialyzer.

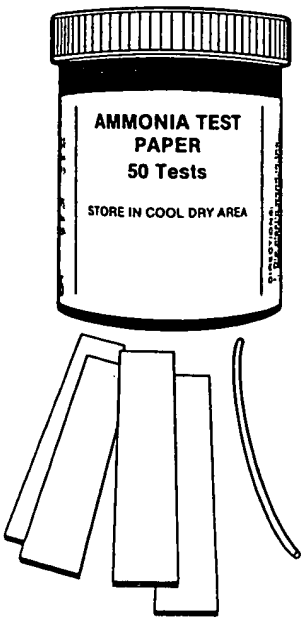


Figure 1.4: Ammonia Test Strips

1.2.E. Ammonia Testing

The ability of the urease layer to convert urea into ammonium carbonate is infinite. However, the capacity of the zirconium phosphate to bind ammonia is finite; eventually all the sites available to bind ammonia may be occupied. If this should occur, ammonia will travel with the Cartridge effluent into the reservoir and eventually to the dialyzer, where it will pass through the membrane into the blood of the patient. Failure to select a Cartridge with sufficient capacity for each patient (see 1.2.F, pg. 6) or to perform ammonia testing during dialysis may result in ammonia toxicity.

For the majority of patients ammonia testing should be performed every 30 minutes during the third hour of dialysis and every 15 minutes thereafter. However, ammonia testing should be done every 15 minutes after the 1st hour of treatment for patients who are: very large (>100 Kg), very catabolic (i.e., high fever, sepsis, etc.), and/or very uremic (SUN >150mg/dl) as such patients generate unusually large amounts of ammonia. Ammonia test strips (Figure 1.4) are available from COBE Renal Care. One test strip will usually suffice for an entire dialysis if different sites are used on the strip for each test.

Obtain a sample of Cartridge effluent by passing one end of the plastic wand, enclosed in each bottle of ammonia test strips, through the stream of cartridge effluent entering near the top of the reservoir (Figure 1.5).

1.2.E. Ammonia Testing (continued)

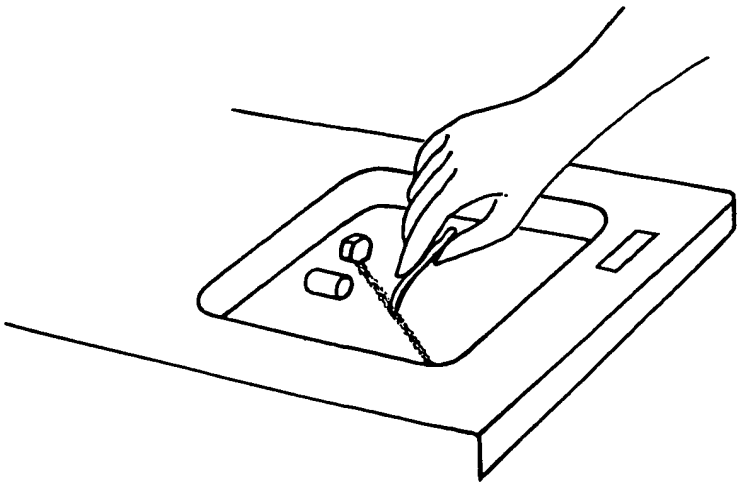


Figure 1.5: Testing the Cartridge Effluent

Touch the tip of the wand to a clean spot on the test strip, allowing the drop to moisten the strip. (Try to handle only one end of the test strip when removing it from its container, as there is some ammonia in normal perspiration.)

Wait 5 minutes, then compare the color of the test strip with the color key on the ammonia test strip container.

If the strip remains white, the Cartridge is still binding all the ammonia being produced.

Pale grey (2 mg%) indicates the capacity has just been exceeded. Change the Cartridge and continue dialysis—or discontinue the treatment, with the machine in CARTRIDGE BYPASS—depending on how near the end of treatment the ammonia breakthrough occurs and your dialysis center's policy for this situation.

A dark grey (5 mg%) test result requires a change of Cartridge **and dialysate** or immediate termination of the dialysis, again depending on timing and dialysis center policy.

Note—a yellow or greenish-grey test result will occur if hyperalimentation or other amino acid-containing solutions are administered into the arterial blood line. This discoloration does not indicate ammonia breakthru but may make it impossible to detect breakthru, should it occur. Since amino acids and other nutrients in hyperalimentation solutions are dialyzable, it is recommended that these solutions always be administered into the venous blood line.

1.2.F. Cartridge Selection

Ammonia breakthrough can usually be prevented if the proper Cartridge is selected or, in extreme situations, the need to change Cartridges mid-dialysis is anticipated. The amount of urea presented to the Cartridge during a specific dialysis depends on many factors, such as the size of the patient, his pre-dialysis SUN (or BUN), the duration of the treatment, and the blood and dialysate flow rates, to name a few.

Graph Method

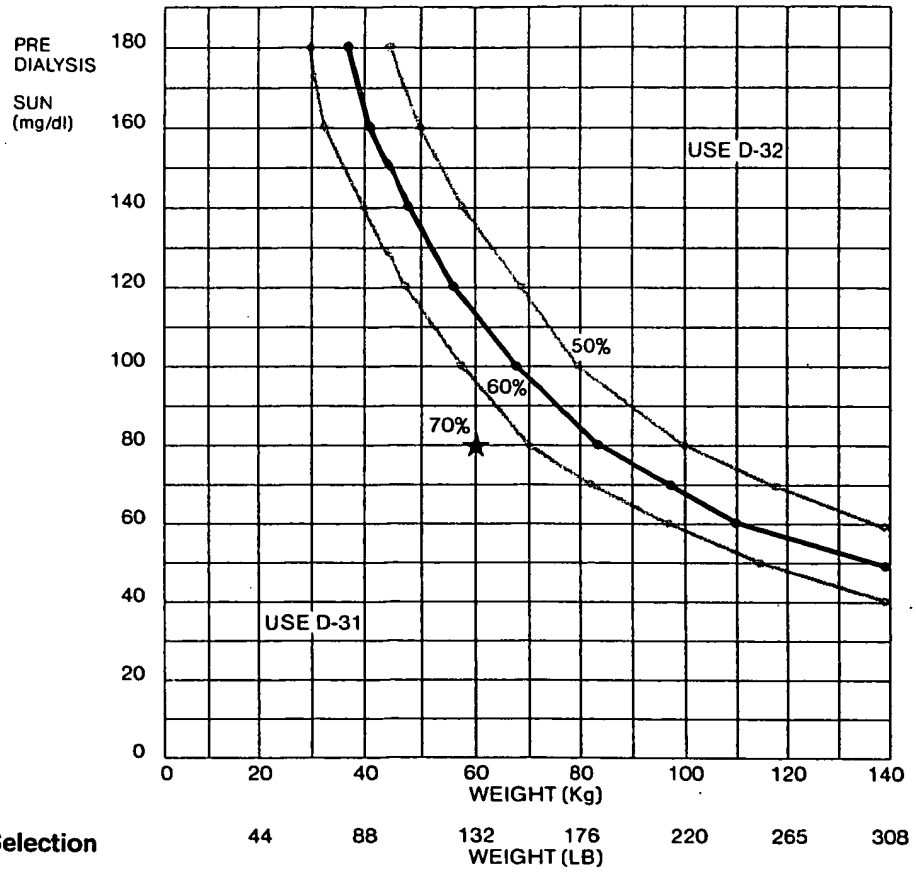
As a general "rule of thumb", the graph on the next page can be used to select the appropriate Cartridge for a given patient (Graph 1.1: Cartridge Selection). Find the point at which the patient's pre-dialysis body weight and SUN values intersect and use the Cartridge size indicated for that zone. The 60% body fluid line should be used as the Cartridge zone divider in most cases, since the body fluid volume (area in which urea is distributed) of the average adult is 60% of the total body volume.

If the patient is very emaciated or very obese, his body fluid volume is likely to be closer to 50% of his body weight. Use the 50% fluid volume line as the separator between the two types of Cartridges.

If the patient is a young child or is an adult with a massive fluid overload (fluid gain greater than 20% of dry body weight), use the 70% fluid volume line as the separator between the two types of Cartridges.

1.2.F. Cartridge Selection (continued)

EXAMPLE:
An adult patient weighs 60 kg and has a pre-dialysis SUN of 80 mg/dl. The patient has average body size, fluid gain, etc. for a dialysis patient. From chart: This patient's parameters (indicated by star) fall within the SORB Cartridge range.



Graph 1.1: Cartridge Selection

Urea-Nitrogen Calculation

However if there is any doubt, for example if the patient's SUN and body weight coordinates fall on the line between the two Cartridges, there is a calculation which can be used to compute the number of grams of urea-nitrogen the patient is likely to present to the Cartridge. The calculation method is provided in Section 5.2.D.

REDY Compute

REDY Compute is a computer program in which patients are modeled for sorbent dialysis. Available in either hand-held microprocessor or disk format, the program asks specific questions about patient parameters, such as predialysis weight, SUN, etc., and desired treatment outcomes (fluid loss, urea reduction, etc.), then displays cartridge selection, dialysis duration and patient blood chemistry outcomes with various dialysates. REDY Compute is available from COBE Renal Care.

1.2.G. Cartridge Capacity: Effect of Dialysate Recirculation.

In addition to urea-nitrogen, the zirconium phosphate layer also adsorbs unused infusate cations (calcium, magnesium, potassium) returning to the Cartridge from the dialyzer. These ions occupy sites on the zirconium phosphate which could otherwise bind urea-nitrogen (ammonia). Provision has been made, with respect to Cartridge capacity, to provide for the infusate ions returned to the Cartridge during a 4-5 hour dialysis.

However, if the system is set up and left recirculating for 30 minutes or longer before dialysis is begun, a substantial additional amount of infusate cations will enter the Cartridge and occupy zirconium phosphate sites. Thus, **recirculating the system prior to initiating dialysis will reduce the urea-nitrogen capacity of the Cartridge**. The Cartridge will lose approximately 1 gram of urea-nitrogen capacity every 40 minutes of recirculation.

If dialysis cannot be initiated within 15 minutes after set-up is completed, we recommend that the system either be turned off or placed in STANDBY/CARTRIDGE BYPASS mode.

1.3 INFUSATE

1.3.A. The Purpose of Infusate

Infusate is a concentrated solution of calcium acetate and magnesium acetate. Potassium acetate, which is optional, may also be included. The infusate chemicals are added by the infusate pump to the Cartridge effluent to produce regenerated dialysate.

At first, the calcium, magnesium and potassium levels in the dialysate reflect the concentration of those chemicals in the concentrate used to make the initial 6 liter bath. When the machine is turned on, the dialysate begins to circulate through the Cartridge and the infusate begins to flow.

The Cartridge removes all of the calcium, potassium and magnesium from the dialysate. By the time the dialysate has circulated through the Cartidge for 60 minutes, regardless of when the patient was connected to the system, the infusate system controls the potassium, calcium and magnesium concentrations in the dialysate. That means the amount of these chemicals in the concentrate used to make the initial 6 liters of dialysate is relatively unimportant, since the patient is usually exposed to the initial bath for less than 30 minutes. Thus any acetate dialysate concentrate that is handy can be used to make the initial 6 liter bath.

The cartridge continues to remove all of the calcium, magnesium and potassium from used dialysate during the entire treatment. An uninterrupted flow of the infusate is necessary to ensure the regenerated dialysate contains the prescribed levels of these chemicals.

1.3.B. Preparation

Infusate is simple to prepare. Each Sorbent Cartridge comes with a pre-measured packet of standard infusate chemicals which is called SORB 10 infusate. The SORB 10 packet contains enough calcium acetate and magnesium acetate so that when its contents are diluted with about 280 ml of warm water (to make 300 ml of solution) and pumped at a preset rate into the effluent coming out of the Cartridge, the resulting dialysate contains 3 mEq/L of calcium and 1 mEq/L of magnesium.

Note that SORB 10 does **not** contain potassium. If prescribed, potassium must be added separately. This is discussed in section 1.3.C.

By way of a helpful hint, the water used to dissolve the infusate chemicals should be approximately the temperature of tepid bath water (90-110°F or 32-43°C). It takes a long time to dissolve the chemicals if cold water is used; very hot water (above 110° F, 43°C) may make the chemicals gummy and difficult to dissolve.

1.3.C. Infusate Additives

The composition of the infusate mixture can easily be modified by varying the infusate chemicals added to the system. The concentration of each chemical can be varied independently by the physician, who is responsible for prescribing dialysate composition.

K-1 Potassium Additive

SORB 10 infusate does not contain any potassium. This is a deliberate omission because some patients require a potassium-free dialysate. When the physician orders potassium in the dialysate, it is added separately to the infusate, using packets of K-1 infusate additive. Each packet of K-1 infusate additive, when added to the infusate mixture, will increase the dialysate potassium (and acetate) by one milliequivalent per liter.

Ca-1/2 Calcium Additive

Sometimes the physician prescribes a dialysate with 3.5 or 4.0 mEq of calcium per liter. Calcium additive packets, Ca-1/2, are available from COBE Renal Care so that dialysate calcium can be increased above the 3 mEq/L provided by the standard infusate mixture, SORB 10. Each packet of Ca-1/2 infusate additive, when added to the infusate mixture, will increase the dialysate calcium (and acetate) by one-half of a milliequivalent per liter.

ces

sates

ians sometimes order fractional amounts of potassium in dialysate: 2.5 mEq/L, for example. l infusates may be prepared as follows:

e one packet of K-1 Infusate Additive in 100 ml of warm water.

sired fraction of the resulting potassium solution in a clean infusate cup. (Example: half of g solution equals 0.5 mEq/L potassium additive.)

e contents of a SORB 10 packet and the desired number of K-1 packets to the cup. (This be two K-1 packets for our example above.)

three-fourths full with warm water (90-110°F or 32-43°C).

ntil mixed.

ater to neck (300 ml total infusate volume).

til dissolved.

the need is less probable, Ca-½ Infusate Additive may be fractionated in the same manner. In of Ca-½ Infusate Additive, keep in mind that half of the resulting calcium solution prepared provides a 0.25 mEq/L Calcium Additive.

nfusates

se SORB 10. Fill the Infusate Jar with dialysate from the reservoir to prevent alarms, and machine as usual. The final dialysate will contain no potassium, magnesium or calcium.

um is prescribed, add the contents of the correct number of K-1 Infusate Additive packets to infusate jar and dilute as usual. The final dialysate will contain potassium but no magnesium n.

sician must decide whether a magnesium-free dialysate is acceptable. If it is not, add 13 g m Acetate to the infusate jar for each 1.0 mEq/L of magnesium ordered, and dilute as usual.

sium Acetate is not available, 12 g Magnesium Chloride may be substituted. Premeasured m Acetate and Magnesium Chloride packets are available from COBE Renal Care. In an cy, the hospital pharmacist or crash cart may be able to provide one of these chemicals.

lysate Flow Rate

te composition is linked to dialysate flow rate. The dialysate flow rate is fixed at 250 ml/min and e adjusted by the operator. The infusate is also preset, at 0.65 ml/min, to accompany a in dialysate flow rate. Both dialysate and infusate flow rates are constantly monitored by the cessor. The recommended infusate dilution must never be changed; to do so may result in a composition different than that ordered by the physician.

Older sorbent equipment, such as the REDY URS and Sorbsystem SSD, had an adjustable flow rate but a fixed infusate flow linked to the dialysate flow rate recommended for that nt (200 ml/min). **No alterations** should be made in dialysate flow rate or infusate dilution nded for that equipment, apart from those contained in this chapter.

PRINCIPLES OF SORBENT DIALYSIS

2.1 VOLUME RELATIONSHIPS

A. Body Fluid Volume

The human body is composed primarily of water. This volume of water is mostly distributed between three body fluid compartments: intracellular fluid, extracellular fluid and blood (intravascular fluid). Water accounts for 60% of the body weight of normal adult males. The average adult female is about 55% water, due to her slightly higher fat content (fat contains no water). Children and certain other people are exceptions to the norm of approximately 60% of body weight being fluid. These exceptions are given in Figure 2.1.

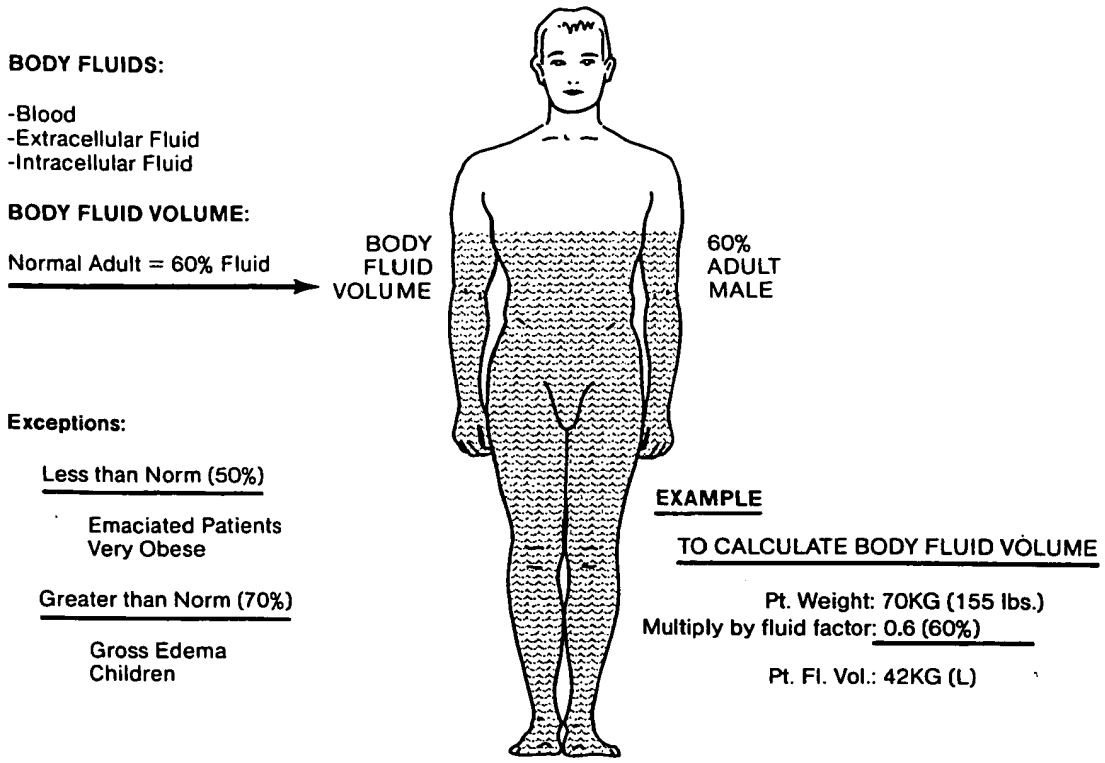


Figure 2.1: Body Fluid Volume

Many chronic hemodialysis patients have a relatively normal body fluid volume. That is, they have little or no significant fat loss or muscle wasting and their interdialytic fluid gains represent an addition of less than 15% of their "dry" body weight. These people have an essentially normal body fluid volume of 60%. However, some chronic and most acute hemodialysis patients are significantly emaciated and/or significantly overhydrated (fluid gain greater than 15%-20% of dry weight). In these people, fluid volume can vary between approximately 50% (emaciated) and 70% (overhydrated) of body weight.

Body fluid volume is important in hemodialysis because the metabolic waste products and electrolytes we wish to remove or balance are distributed throughout the body fluids. The blood stream is used to access the entire body fluid volume of the patient, and to measure the results of the treatment.

B. Volume Relationship in Single Pass Dialysis

Hemodialysis is accomplished by applying: (1) a **concentration gradient** between blood and dialysate across a semi-permeable membrane in order to alter the chemical composition of the body fluid, and (2) a **pressure gradient** across the semi-permeable membrane in order to remove excess fluid from the body, if necessary.

There are some differences between how single pass (i.e., proportioning pump) and Sorbent Dialysis Systems work with respect to concentration gradients, which, when understood, can be used to benefit the patient. (There is no difference between the two systems with respect to ultrafiltration.)

These differences are due to the differing total volumes of dialysate to which the fluid volume of the patient is exposed during the course of dialysis on each system.

2.1 VOLUME RELATIONSHIPS (continued)

This can best be explained by considering what happens to the "average man" (i.e., body weight 155 lbs or 70 kg with a fluid volume of 60% of body weight or 42 L).

During a typical 4 hour dialysis on a single pass system, our "average man" is exposed to 120 L of dialysate (500 ml/min x 240 min). Since this volume of fluid and electrolytes is approximately three times the 42 L fluid volume of the "average man", his chemical composition changes to match that of the dialysate (Figure 2.2: Volume Relationships: Single Pass). That is, the dialysate controls the patient. As long as the chemical composition of the entire 120 L of dialysate remains safe, i.e within normal human chemistry range, the patient benefits. Any deviation from the "safe" range may cause harm, even death.

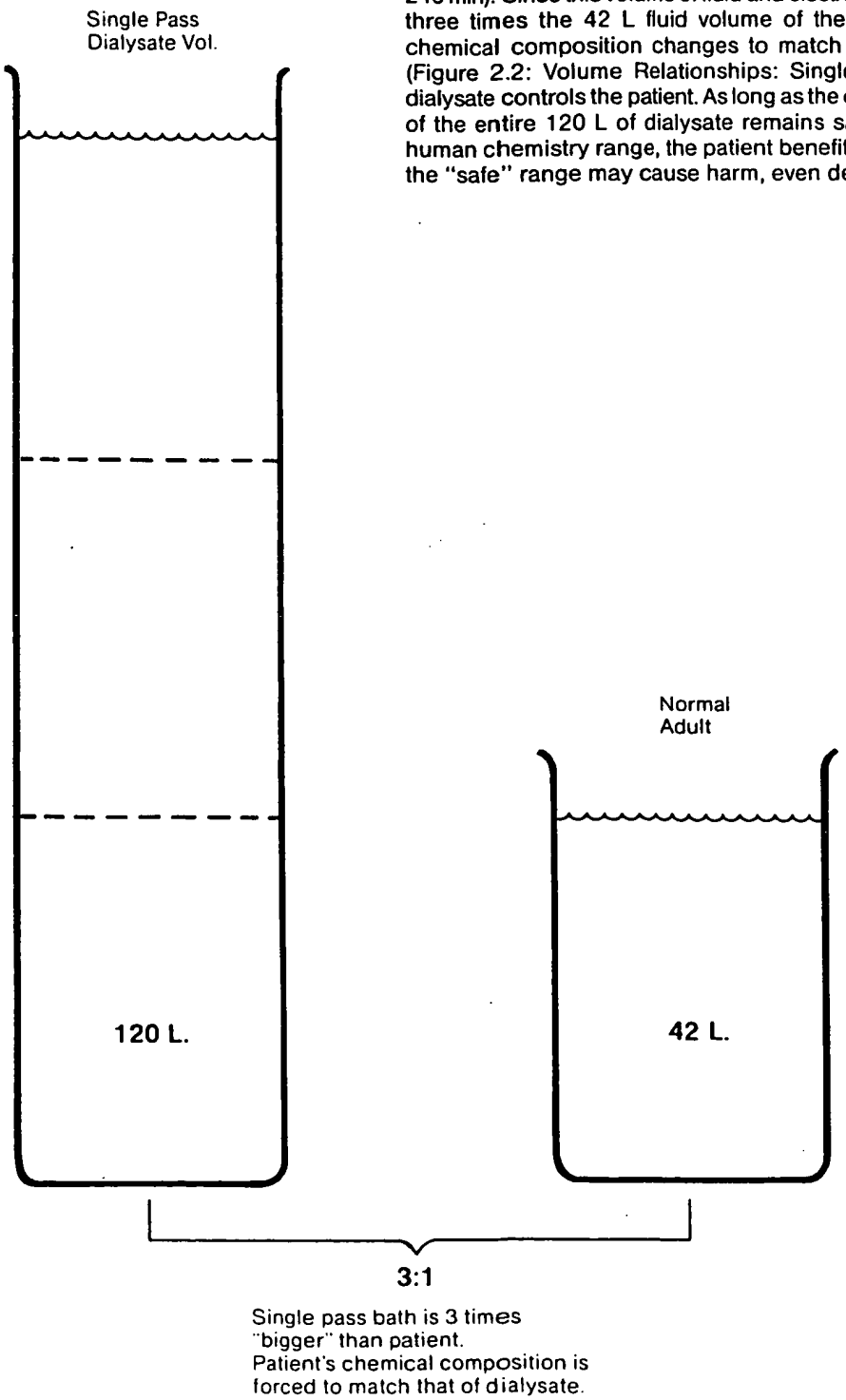


Figure 2.2: Volume Relationship: Single Pass

C. **Volume Relationship in Sorbent Dialysis**

During a typical 4 hour Sorbent dialysis, our "average man" is exposed to 6 L of dialysate which is continuously regenerated. The patient, at 42 L, is approximately 7 times the volume of the dialysate (Figure 2.3: Volume Relationship: Sorbent Dialysis). Except for those substances the Cartridge removes or donates (urea, sodium, etc.), the **patient** controls the composition of the dialysate. Furthermore, should changes occur in the dialysate composition (increased sodium level, for example), the change would have to be quite large before it could have a significant effect on the patient's chemistries.

The dialysate sodium concentration would have to change by 7 mEq/L in order to achieve a 1 mEq/L change in the serum sodium of our "average man". This is because at 42 L, he contains 7 times more volume than the 6 L volume of the dialysate. Recall that when sodium crosses the dialyzer membrane into the patient, all of it does not remain in the blood stream. Instead, the sodium is distributed throughout the body fluids.

For example, if each liter of dialysate transferred 7 mEq of sodium (6 L x 7 mEq/Na/L = 42 mEq Na) into the much larger fluid volume of the "average man's" body, his sodium level would rise only 1 mEq/L (42 mEq Na divided by 42 L = 1 mEq/L).

Conversely, our "average man" can cause a low dialysate sodium to rise without giving up an appreciable amount of his own body sodium. For example, suppose our "average man" had a sodium of 136 mEq/L and was exposed to a Sorbent System dialysate containing only 120 mEq/L sodium. He need give up only 2 mEq/L of his sodium to force the dialysate to equilibrate with him (see Section 2.3.B.). The patient's sodium would drop to 134 mEq/L while the dialysate, receiving 84 mEq of sodium (42L x 2 mEq), would rise to 134 mEq/L (84 mEq divided by 6L, added to the original 120 mEq/L). The patient controls the dialysate sodium by virtue of his larger volume.

The unique design of Sorbent Dialysis Machines (small dialysate volume in a closed system) results in a volume relationship which protects the patient from significant changes in dialysate composition.

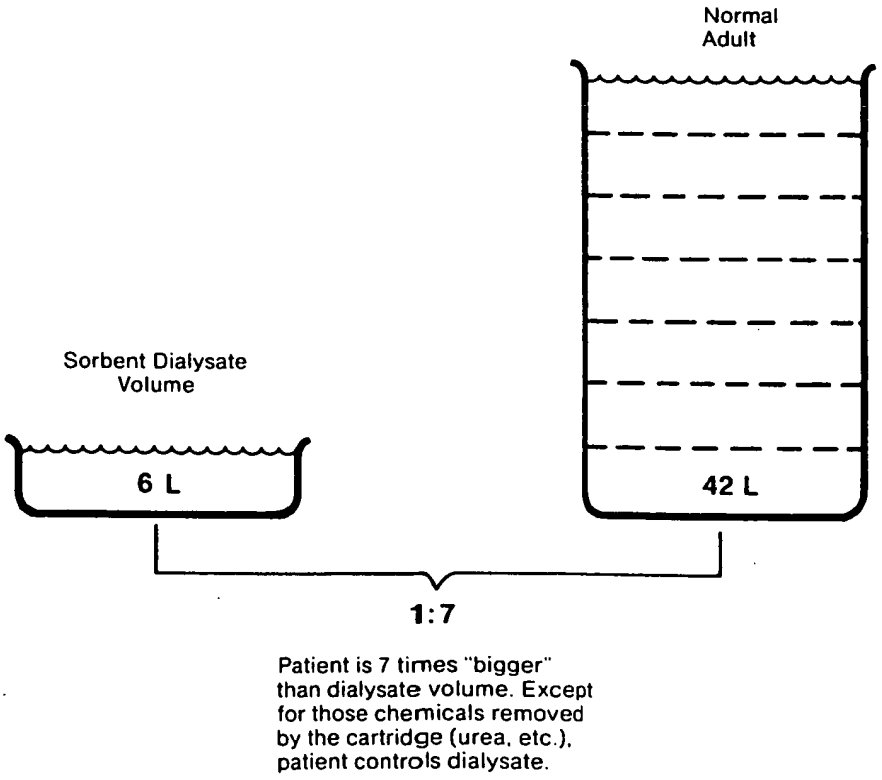


Figure 2.3: Volume Relationship: Sorbent Dialysis

D. **Implications of Volume Relationships**

When one is dealing with a very small volume of dialysate in a closed system, large swings in dialysate sodium concentration have very little effect on an adult patient with a normal serum sodium. The volume relationship between the patient and the dialysate is a potential source of safety in Sorbent Systems.

In fact, the achievement of significant alteration in patient sodium levels requires very large and sustained changes in dialysate sodium concentration. The methods for achieving these changes are discussed in Section 2.3.C., Manipulation of Patient Sodium.

2.1 VOLUME RELATIONSHIPS (continued)

Also, other substances which are either "transparent" to or emitted by the Cartridge are conserved in much the same way as sodium. Some examples are chloride, acetate and glucose.

2.2 HOW SORBENT DIALYSIS SYSTEMS CHANGE DIALYSATE

The dialysate composition during a Sorbent Dialysis does not remain constant. Cartridge and patient may be adding or subtracting various substances during dialysis, and the infusate system is constantly adding calcium, magnesium and potassium. These changes should be considered and used to facilitate the treatment of the patient.

Sodium
The initial dialysate for most chronic patients is prepared with a sodium concentration of 100-110 mEq/L. Additional sodium enters the dialysate from the dialyzer saline prime and from unadsorbed sodium in the Cartridge. During dialysis, further amounts of sodium are added to the dialysate by the Cartridge in exchange for urea, calcium, magnesium and potassium so that at the end of dialysis, the sodium concentration of the dialysate is usually greater than 150 mEq/L. These changes in dialysate sodium concentration are not transmitted to the patient to any meaningful degree (see Section 2.1, Volume Relationships) and may be beneficial; however fixed dialysate sodium levels can also be maintained (see Section 2.3, Sodium Dynamics).

Initial sodium concentrations as low as 90 mEq/L have been utilized to increase sodium loss by the patient, and concentrations as high as 160 mEq/L have been utilized to donate sodium to patients with severe hyponatremia. Detailed instructions in the technique of adjusting patient sodium levels are provided in Section 2.3.C. Table 2.2 on page 20 gives the amount of acetate concentrate to use to obtain various initial sodium concentrations.

Chloride
The chloride concentration in the initial dialysate is fixed by its relationship to the sodium in the concentrate. With an initial starting sodium of 100-110 mEq/L, the initial chloride concentration is approximately 80 mEq/L (and about 25 mEq/L acetate). Additional chloride is added to the dialysate by the saline prime, and during dialysis chloride is donated by the patient until the dialysate equilibrates with the serum chloride.

Potassium
The potassium concentration of the initial dialysate depends upon the concentrate used and its dilution. Passage of the dialysate through the Cartridge removes all potassium so that the dialysate level will equal approximately the average of the initial dialysate and infusate concentrations one-half hour after dialysate flow has begun and will equal that of the infusate alone in approximately one hour. Thus for the major portion of the dialysis, the potassium level is determined solely by the infusate.

The potassium clearance possible with the system often permits setting the infusate potassium level at about 1 mEq/L less than that used with single pass dialysis on the same patient. The patient's potassium needs should be evaluated to determine the appropriate levels required in the infusate.

Calcium and Magnesium
The initial level of calcium and magnesium in the dialysate depends upon their amount in the concentrate, the dilution of the concentrate, and the amount in the tap water used to prepare the dialysate. One-half hour after dialysate begins to flow through the machine, the concentration of calcium and magnesium will equal the average between the initial dialysate and the infusate levels; it will be equal to the infusate concentration in one hour. Thus, the calcium and magnesium level in the dialysate are dependent primarily upon the infusate.

Acetate
The initial acetate concentration in the dialysate depends upon dialysate concentrate and its dilution. An initial dialysate made of one packet of Dry Acetate Concentrate* or 135 ml standard acetate dialysate concentrate added to 6 liters of water contains about 25-30 mEq/L acetate. During the course of dialysis, the infusate provides acetate as well as calcium, magnesium and potassium. Further quantities of acetate are provided by the Cartridge in exchange for phosphate. At the same time, acetate is dialyzed into the blood and converted to bicarbonate. A combination of all these factors results in a dialysate acetate concentration between 15 and 20 mEq/L at the end of dialysis. Patients vary considerably in their ability to convert acetate to bicarbonate. With high efficiency short time dialysis, conventional dialysis systems may provide excessive acetate. Patients on the Sorbsystem receive much less acetate than patients on other systems (see Section 2.4, Acetate Dialysate).

*Available from COBE Renal Care

2.2 HOW SORBENT DIALYSIS SYSTEMS CHANGE DIALYSATE (continued)

Bicarbonate
The initial bicarbonate level of the acetate dialysate is zero. During the early part of the dialysis, the patient donates bicarbonate to the dialysate, some of which is converted to CO_2 and water by the zirconium phosphate in the Cartridge. The patient donates urea, of which 10-20% is converted to sodium bicarbonate by the Cartridge. This results in an increase in the bicarbonate level of the dialysate to 10-20 mEq/L within the first two hours of dialysis. Subsequently, the dialysate bicarbonate increases slowly while remaining in equilibrium with the increasing serum bicarbonate.

Phosphate
The phosphate level in the dialysate is maintained near zero. Phosphate donated to the dialysate by the patient is completely removed by the Sorbent Cartridge.

Glucose (Dextrose)
The glucose level of the initial dialysate depends upon the concentrate used and the dilution. Subsequently, glucose moves across the dialyzer membrane in either direction, depending upon the concentration gradient. Within approximately two hours, the concentration of the dialysate equilibrates with that of the blood. The dialysate-Cartridge combination then acts as a buffer to prevent sudden changes in glucose concentration.

pH
The pH of the initial dialysate depends upon the pH of the concentrate and water used for dilution. When the Cartridge is inserted, there may be a slight initial increase in pH due to a small amount of sodium compounds being adsorbed. Subsequently the pH will drop due to the formation of carbon dioxide. The pH will eventually rise toward neutral.

CO_2
Early in the dialysis the patient donates carbon dioxide and bicarbonate to the dialysate. Additional amounts of carbon dioxide are formed from bicarbonate and from urea conversion. The carbon dioxide prevents the precipitation of calcium. Also, dissolved air is removed from the dialysate as the carbon dioxide leaves the dialysate reservoir.

2.3 SODIUM DYNAMICS

2.3.A. Sources of Dialysate Sodium

With single pass dialysis systems, the dialysate sodium concentration depends completely upon the composition of the dialysate concentrate and the amount of dilution. However, with Sorbent Dialysis the dialysate sodium concentration varies during the dialysis and depends upon many factors.

Initial Dialysate
Initially, the sodium concentration depends upon the dialysate concentrate dilution. For the stable patient, a starting dialysate of 110-120 mEq/L of sodium is recommended. Such a dialysate is prepared by diluting one packet of Dry Acetate Concentrate* or 150 ml of any commercially available liquid acetate concentrate in 6.0 liters of water.

Saline Prime
Dialyzers are usually primed with normal saline which has a sodium concentration of 155 mEq/L. Dialysis between the saline prime and the dialysate can take place. The sodium from one liter of saline can increase the dialysate sodium concentration by 8 mEq/L if the saline prime (1 liter) is completely dialyzed. Normally 3-5 mEq/L is the average increase seen, since a saline prime of 500 ml is most commonly used and not all of the sodium is dialyzed.

Initial Cartridge Equilibration
When dialysate is first passed through the Sorbent Cartridge, there is about a ten minute period of equilibration during which up to 50 mEq of sodium is released from the Cartridge into the dialysate, thereby increasing the dialysate sodium concentration by 8-9 mEq/L.

New Sodium Concentration at Onset of Treatment
In any system which is characterized by Sorbent regeneration of a fixed amount of recirculated dialysate, the sodium in the initial dialysate should be low (120 mEq/L) in order to accommodate the sodium which enters it from the saline prime (3 mEq/L) and initial Cartridge equilibration (8 mEq/L). Thus when the patient goes on dialysis the dialysate sodium will total about 130 mEq/L.

*Available from COBE Renal Care.

2.3 SODIUM DYNAMICS (continued)

This seemingly low dialysate sodium at the beginning of the treatment is normal and desirable in Sorbent dialysis. It, in effect, "leaves room" for the sodium continuously emitted by the Cartridge in exchange for the waste products it removes from the recirculated diaysate throughout the dailysis. This process is described in the next section.

Sources of Dialysate Sodium Increase During Dialysis

Infusate
The calcium, magnesium and potassium levels of the six liter dialysate bath are maintained by the infusate system at a level of: calcium = 3 mEq/L, magnesium = 1 mEq/L (if SORB 10 is used), and potassium (K-1) as prescribed (usually from 0 to 4 mEq/L). The entire contents of the reservoir (6 L) moves through the dialyzer (and the Cartridge) twice each hour (dialysate flow of 200 ml/min x 60 min = 12 L). For the REDY 2000, the figure would be 15 L/hr (250 ml/min x 60 min). So the infusate must be added at a rate that provides 6 mEq/L of calcium and 2 mEq/L magnesium each hour. Potassium, if present, is added at a rate of 2 mEq/L per hour for each 1 mEq/L in the dialysate. In the Cartridge, these ions are exchanged for sodium. Thus the dialysate sodium can increase about 10 mEq/L per hour from this source (6 from calcium, 2 from magnesium and 2 for each 1 mEq/L of potassium). For the REDY 2000, this figure would be 12.5 mEq/L (7.5 from calcium, 2.5 from magnesium and 2.5 for each 1 mEq/L of potassium).

Urea/Sodium Exchange
As the patient's urea enters the Cartridge, it is converted to ammonium carbonate by the urease layer. The ammonium ions are adsorbed by the zirconium phosphate; about 15% are exchanged for sodium and 85% for hydrogen ions. Subsequently the hydrogen ions combine with the carbonate to form bicarbonate, carbon dioxide, and water.

In a usual dialysis, about 17 grams of urea nitrogen are adsorbed by the Cartridge during a four hour treatment. This will produce an approximate sodium gain of 7.5 mEq/L per hour. The anticipated sodium increase can be calculated as follows:

GIVEN:

17 gms urea-nitrogen is the assumed amount of urea-nitrogen presented to the Cartridge (in this example)
14 gm/mole is the formula weight of nitrogen
.15 is the average percent conversion of urea to sodium bicarbonate by the Cartridge
1000 is the conversion from Eq to mEq

STEP 1

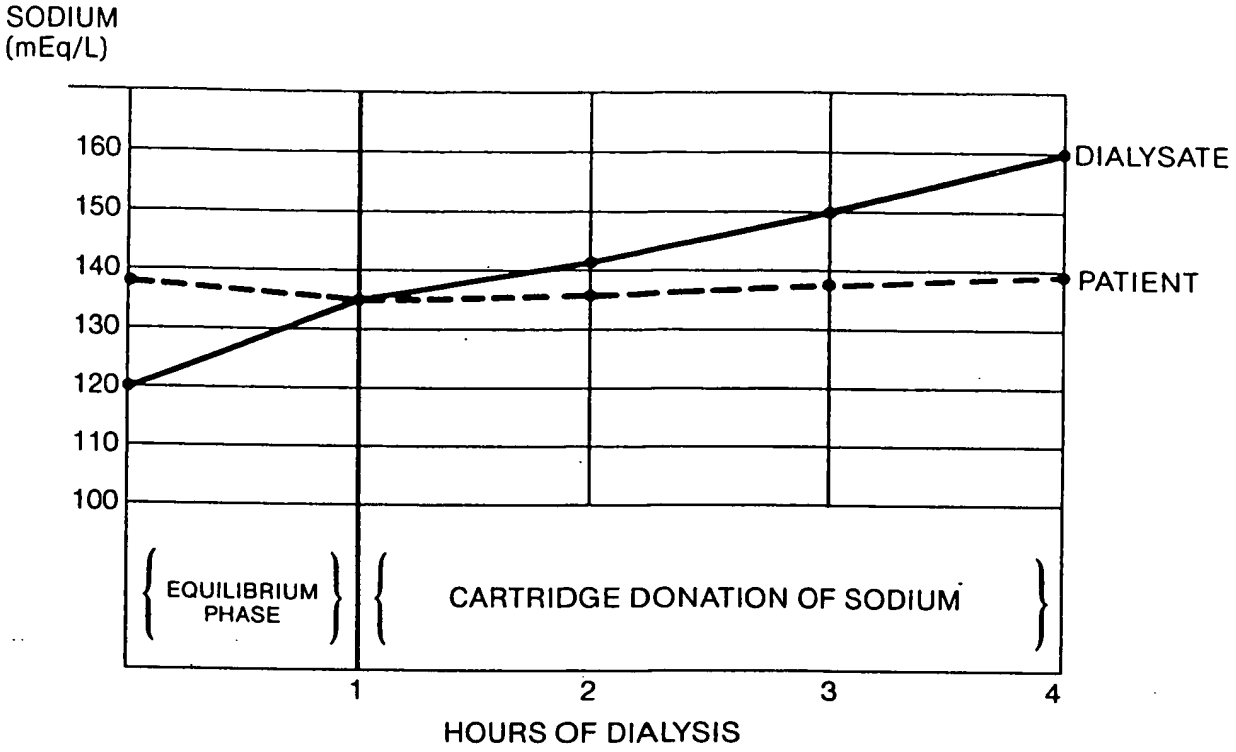
$$\frac{17 \text{ gms urea-nitrogen}}{14} \times .15 \times 1000 = 182 \text{ mEq total amount sodium produced}$$

STEP 2

$$\frac{182 \text{ mEq sodium}}{4 \text{ hours}} \text{ divided by } 6 \text{ liters dialysate} = 7.5 \text{ mEq sodium/L/hour}$$

2.3.B. Effects of Variable Dialysate Sodium

1. **Equilibration Phase**
In the first 40-60 minutes, the patient donates some of his sodium to the dialysate until equilibrium occurs. Assume, for example, the patient's body fluid volume is 42 L, or is seven times bigger than the volume of dialysate, and his pre-dialysis sodium is 135 mEq/L versus an initial Sorbent dialysate sodium of 120 mEq/L. To reach equilibrium the patient would transfer about 2 mEq of sodium from each of his 42 liters of body fluid into the smaller volume of dialysate. This increases the dialysate sodium by 14 mEq/L (42 x 2 mEq divided by 6 L). The equilibrium point, in this case would be 134 mEq/L. These changes are illustrated in the first segment of the graph in Graph 2.1: Patient Sodium vs Dialysate Sodium.



Graph 2.1: Patient Sodium vs Dialysate Sodium

2. **Cartridge Donation of Sodium**
During the subsequent three hours of treatment, the Cartridge releases sodium in exchange for adsorbing urea-nitrogen, calcium, magnesium and potassium. Dialysate sodium, and thus conductivity, begins to rise.

The amount of sodium produced each hour varies with the amounts of urea, calcium, magnesium and potassium presented to the Cartridge by the used dialysate. Using the figures from page 16 for the sodium generated from an average infusate and an average urea-nitrogen as a guideline, the amount of sodium added to the dialysate each hour ranges between 15-20 mEq/L.

However, due primarily to the difference in volume between patient and dialysate, the slower dialysate flow rate (compared to single pass systems), and the time required for distribution of sodium throughout the larger volume of the patient, only about half of the sodium generated per hour enters the patient. For the average adult, this amounts to a sodium increase of approximately 1 mEq/liter/hour.

The rest of the sodium accumulates in the dialysate, resulting in a conductivity increase of about 1 mMho/hour (or an increase of about 10 mEq sodium/liter/hour).

Thus the average adult renal patient with a normal or near normal pre-dialysis sodium will complete a 3-5 hour standard Sorbent dialysis (initial dialysate sodium of 120 mEq/L) with a sodium at or within 2-3 mEq/L of his pre-dialysis level—despite dialysate sodium levels that rise continuously throughout the dialysis to levels which may be considered hypertonic in single pass systems.

The increasing disparity between the sodium levels of patient and dialysate after the first hour of dialysis is illustrated in Graph 2.1, Patient Sodium vs Dialysate Sodium.

Note that this discussion applies to the normonatremic patient only. For a discussion of patients presenting with hyponatremia or hypernatremia, please turn to section 2.3.C.

For more precise information, including mathematical models of the sodium dynamics of Sorbent Dialysis, please turn to Appendix 5.2.A.

2.3.B. Effects of Variable Dialysate Sodium (continued)

Dialysate Flow Rate and Sodium

The maximum allowable Dialysate Flow Rate (DFR) of Sorbent Dialysis is 250 ml/min, as compared to a 500 ml/min DFR with single pass systems. This lower dialysate flow decreases the rate of sodium clearance. Despite the sodium concentration gradient that is present with Sorbent regenerative dialysis, the end result is that due to the volume relationship, the patient will experience a gradual, controlled loss of sodium to the dialysate during the equilibration phase and slowly regain the lost sodium during the latter part of the treatment. This rise in body sodium may protect the patient from the muscle cramps and hypotension often experienced during the last hour of the treatment with single pass dialysis.

A Few Words About Ultrafiltration

Because the ultrafiltrate that is lost during the dialysis treatment has the same sodium concentration as the patient, it may produce a change in the dialysate sodium concentration, i.e., if the patient's sodium level is significantly lower than the dialysate, a dilution of the dialysate will occur, resulting in a drop in the conductivity reading. If the patient's sodium level is high, the reverse will occur and the conductivity readings will increase signifying an increase in dialysate sodium concentration.

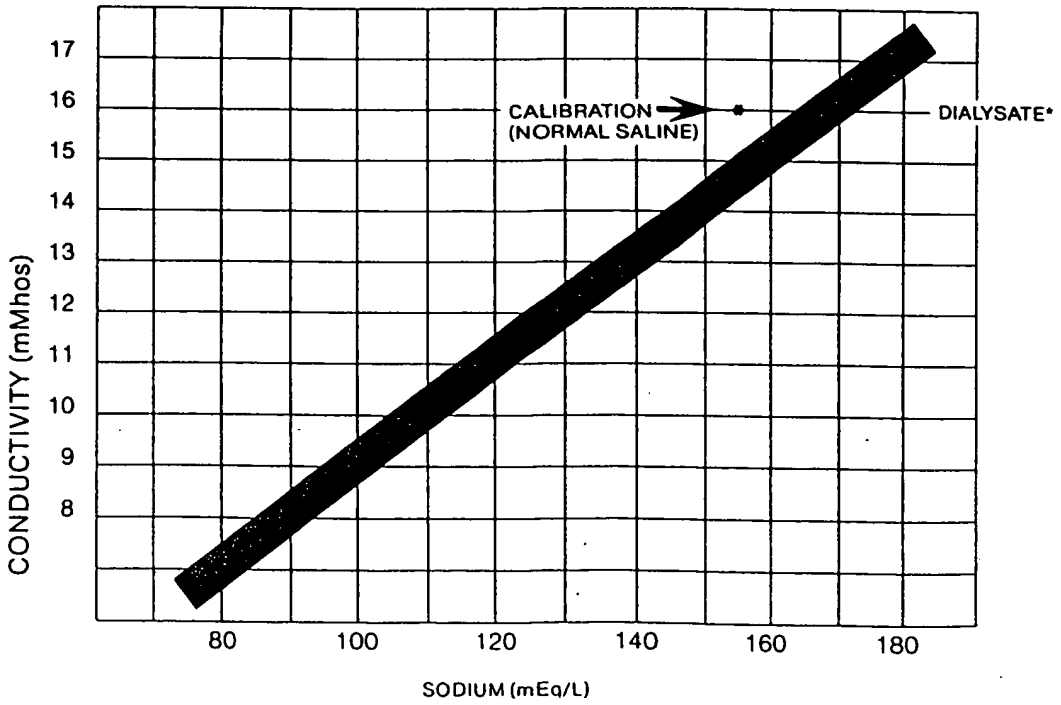
Conductivity as an Indicator of Dialysate Sodium

Conductivity is the measurement of the ease with which an electric current will flow between two electrodes placed in an electrolyte solution, such as dialysate. Electrolytes are salts, which dissociate (break apart) into anions (negative ions) and cations (positive ions) when dissolved in water. The greater the concentration of electrolytes present, the higher the conductivity. An electrolyte solution with a specific chemical composition, such as dialysate, has a known and characteristic conductivity.

Dialysate contains several kinds of cations (ions with a positive charge): sodium, potassium, calcium and magnesium. Potassium, calcium and magnesium are present in only small amounts, a few milliequivalents per liter. Sodium, at 120-155 mEq/L, is by far the most concentrated cation in dialysate. Thus the conductivity meter is essentially reflecting the sodium concentration of dialysate. (A change in dialysate potassium concentration from zero to four mEq/L, for example, is so insignificant compared to the amount of sodium in the bath that it causes no perceptible change in dialysate conductivity.)

Therefore, the conductivity reading can be used as a general indicator of dialysate sodium concentration. The following graph has been prepared as an aid in estimating dialysate sodium concentration at various conductivity readings.

CAUTION: Always verify proper functioning of a dialysis machine conductivity meter by comparing its reading against that of a properly calibrated external conductivity meter. **Do not use this chart to estimate sodium levels unless the machine's conductivity reading has been properly verified.**



*CONTAINING PRIMARILY SODIUM CHLORIDE, ACETATE, AND BICARBONATE

Graph 2.2: Sodium Concentration vs Conductivity

2.3.B. Effects of Variable Dialysate Sodium (continued)

Contribution of Anions

Anions (chloride, acetate and bicarbonate) can also affect dialysate conductivity. Standard dialysates contain about 30-35 mEq/L acetate or bicarbonate and 100-105 mEq/L chloride. Organic anions, such as acetate and bicarbonate, are less efficient conductors of electricity than inorganic anions (chloride). Thus the conductivity of the standard dialysate is somewhat lower than it would be if it contained only sodium and chloride ions. This is why the sodium chloride calibration solution in Graph 2.2 gives a higher conductivity reading than dialysate even though both contain an identical amount of sodium.

This is also why the line on the Sodium vs Conductivity graph is so wide. For example, dialysates giving a conductivity reading of 12 mMhos usually have a sodium concentration of about 127 mEq/L. But the sodium concentration could fall anywhere between 122-131 mEq/L depending on the exact levels of chloride, acetate and/or bicarbonate ions in a given dialysate.

2.3.C. Manipulation of Patient Sodium

The standard Sorbent dialysate described in the preceding section is designed to maintain the body sodium levels of patients with normal, or near normal, serum sodiums. This encompasses most chronic hemodialysis patients and some patients being treated for acute renal failure.

However there are situations, usually in treating acute renal failure patients, where the pre-dialysis serum sodium is not normal. **The standard Sorbent dialysate used for patients with normal serum sodium will not correct significant sodium abnormalities in an adult and should not be used for patients with such abnormalities.** Instead the standard procedures for the patient with hyponatremia or the patient with hypernatremia should be employed.

Standard Procedure: Hypernatremia

With mildly hypernatremic patients (Na 145-150 mEq/L) the dialysate should be maintained at a sodium concentration of approximately 135 mEq/L by adding sufficient water to restore a conductivity of 12.5 mmhos* whenever the conductivity rises above 13.0 mmhos. It is recommended that 2.5 ml of infusate be added to each liter of water used to adjust dialysate conductivity.

*NOTE: Before performing sodium manipulations, the dialysate conductivity should be checked with a properly calibrated external meter to verify the accuracy of the machine conductivity meter.

For more severely hypernatremic patients (Na above 150 mEq/L), it is important that the sodium concentration be lowered slowly since a rapid fall in serum osmolality, due to a rapid drop in sodium, may cause excessive intracranial pressure.

The sodium level selected for the initial 6 L of dialysate should be higher than that of the standard sorbent dialysate for chronic patients. Keeping in mind it may be undesirable to lower the patient's sodium to normal in one treatment, a desired post dialysis serum sodium should be selected. The initial dialysate sodium level and conductivity should reflect this objective. Table 2.1 provides guidelines for dialysate sodium and conductivity levels used to normalize serum sodium.

TABLE 2.1: Normalization of Serum Sodium

PATIENT		RECOMMENDED DIALYSATE	
CONDITION	PRE-DIALYSIS SERUM SODIUM (mEq/L)	SODIUM (mEq/L)	CONDUCTIVITY (mmhos)
Severe Hypernatremia	Over 150	Serum Minus 10	
Mild Hypernatremia	145-150	135-140	12.5-13.0
Normal Sodium	135-144	140-150	13.0-14.0
Mild Hyponatremia	130-134	150-155	14.0-14.5
Moderate Hyponatremia	125-129	155-160	14.5-15.0
Severe Hyponatremia	Below 124	Serum Plus 15	

EXAMPLE:

You need to dialyze a patient for four hours. The patient's serum sodium is 149. The physician left orders to maintain conductivity at 12.5-13.0 throughout the dialysis. To do this, follow these steps:

1. Mix a dialysate with an initial sodium of 120 mEq/L (extrapolated from Table 2.2, a 120 mEq/L initial bath sodium = 155 ml concentrate + 6 liters water). Recall that an additional 5 mEq/L sodium will come from the saline prime and 10 mEq/L will come from the initial Cartridge equilibration. This amount of sodium entering the initial bath will provide a dialysate Na of 135-140 mEq/L. The conductivity

2.3.C. Manipulation of Patient Sodium (continued)

meter should read approximately 12.5 mMhos just prior to initiating dialysis.

NOTE: This level of initial dialysate sodium was chosen to produce a gradual decrease in the patient serum sodium concentration, in order to prevent a rapid decline in the serum osmolality.

2. Initiate the treatment as soon as the temperature is within safe limits.

3. Monitor conductivity throughout dialysis treatment closely.

4. When conductivity exceeds 13.0 mMhos, remove 500 ml of dialysate from the reservoir and replace it with 500 ml of warm (37°C) water.

5. Wait 2-3 minutes for altered dialysate solution to equilibrate, then read conductivity level.

6. If conductivity decreases to desired level (at or slightly below 12.5 mMhos, in this example), continue steps 3-5 throughout dialysis, as necessary. If conductivity does not decrease sufficiently, repeat steps 4 and 5 using smaller volumes of fluid until desired level is reached.

NOTE: Add 1 ml of infusate to the 500 ml of warm water if conductivity adjustments must be performed more than once per hour, in order to provide adequate calcium, magnesium and potassium.

Table 2.2: Concentrate Volume vs Initial Dialysate Sodium

PREPARATION OF DIALYSATE WITH VARIOUS SODIUM CONCENTRATIONS		
LIQUID CONCENTRATE[1] Add Amount Indicated To 6 L Water.	APPROXIMATE DIALYSATE SODIUM	CONCENTRATED SALT SOLUTION[2] Add Amount Indicated To 1 Packet Dry Acetate Dialysate Dissolved In 6 L Water.
ml	mEq/L	ml
155	120	0
170	130	13
185	140	26
200	150	39

[1] Based on commercial acetate concentrate that would yield dialysate sodium of 135 mEq/L at 34:1 dilution in single pass dialysis machines.

[2] Made by adding 21 g NaCl to exactly 80 ml water or 1 packet Dry Acetate Dialysate to 160 ml water; 13ml of either solution contains 60 mEq sodium/(10mEq/L when added to 6 L bath).

Standard Procedure: Hyponatremia
Mild to moderate hyponatremia (Na between 125-135 mEq/L) can safely be corrected during a single dialysis. To do so, an increase in the initial dialysate sodium concentration will be required. This increased sodium (and conductivity) is then maintained throughout the treatment by the periodic addition of small quantities (10-15 ml) of liquid concentrate or concentrated salt solution (21 g NaCl dissolved in 80 ml water **or** 1 packet Dry Acetate Dialysate dissolved in 135 ml water). Use Table 2.1 as a guide to the selection of the desired dialysate sodium level and the information in Table 2.2 to prepare the initial 6 liter bath.

In contrast to mild or moderate degrees of hyponatremia, **rapid correction of severe hyponatremia (Na below 125 mEq/L) may be unsafe. Consult with a physician** before attempting to normalize the serum sodium of a severely hyponatremic patient within a single treatment.

NOTE: Before performing sodium manipulations, the dialysate conductivity should be checked with a properly calibrated external meter to verify the accuracy of machine conductivity meter.

2.3.C. Manipulation of Patient Sodium (continued)

EXAMPLE:

You need to perform a four hour dialysis treatment with a primary goal of increasing the patient's serum sodium level from 125 mEq/L to 135 mEq/L. To do this, follow these steps:

1. Begin dialysis treatment with a dialysate sodium of 145 mEq/L (190 ml liquid acetate + 6 liters water) and the prescribed infusate (SORB 10 plus K-1 and/or Ca-1/2). Recall that the initial "prime through" of the Cartridge will contribute 10 mEq/L sodium to the dialysate. In this example (initial bath sodium = 145 mEq/L) there is only a small gradient between the initial dialysate and the priming saline (155 mEq sodium/L), thus little additional sodium is contributed by this source. Once the dialyzer and machine are entirely primed, the bath sodium should be about 155 mEq/L. The Conductivity meter should be reading 14.5 mMhos.
2. Initiate treatment as soon as the temperature is within safe limits.
3. Every 30 minutes during the dialysis assess machine conductivity reading.
4. If conductivity has dropped below 14.0 mMhos, add 5-10 ml liquid dialysate concentrate **OR** concentrated salt solution (formula in Table 2.2, Note 2).
5. Wait 2-3 minutes for altered dialysate solution to equilibrate, then read conductivity level.
6. If conductivity has increased to desired level (14.5 mMhos or slightly above, in this example), continue steps 3-5 throughout dialysis. If conductivity does not increase sufficiently, repeat steps 4 and 5 until desired conductivity level is achieved.

2.4 ACETATE DIALYSATE

2.4.A Standard Acetate Bath

The standard acetate dialysate is made by adding one packet of Dry Dialysate or 155 ml of any standard dialysate concentrate to 6 liters of tap water. The resulting mixture is circulated through the Cartridge while the dialyzer and bloodlines are saline primed. The Cartridge and priming saline alter the composition of the initial dialysate somewhat (see Section 2.3.A.) so that when the patient is connected to the machine the dialysate composition is approximately the following:

CATIONS	(mEq/L)	ANIONS	(mEq/L)
Na	130	Cl	100
K	1	Acetate	35
Ca	3		
Mg	1		
	135		135

*Assumes a 1.0 mEq/L potassium concentrate. Potassium and chloride levels may be 1-3 mEq/L higher depending on their levels in the concentrate used to make the initial dialysate.

The above values are an approximation because (1) the 6 liter volume of tap water used to dilute the chemical concentrate is not precisely measured and (2) the length of time the initial dialysate mixture is recirculated through the dialyzer and Cartridge prior to patient connection is highly variable. The effect of using somewhat more or less than 6 liters of water to dilute the concentrate is negligible, unless a gross error of measurement (1/2 L or more) has occurred.

The longer the system recirculates, the more the infusate, rather than the initial dialysate concentrate, controls the calcium, magnesium and potassium composition of the dialysate.

After dialysis begins, the level of acetate in the dialysate will decrease slightly and bicarbonate will enter the system. Thus, even though the dialysate was originally made from an acetate concentrate, the patient is exposed to a dialysate which contains both acetate and bicarbonate.

The sources of acetate and bicarbonate and the effects of the resulting acetate/bicarbonate dialysate on the patient are discussed in the following sections.

2.4.B Sources of Acetate

With a standard acetate bath, the amount of acetate in the original 6 liters of dialysate is very small, only about 210 mEq. Since the patient has no acetate in his blood or body fluids and his fluid volume is much larger than the 6 L volume of the dialysate, the acetate in the dialysate will move across the dialyzer

2.4.B. Sources of Acetate (continued)

membrane into the patient. The patient will gradually convert the acetate into bicarbonate. However, the bicarbonate deficit in a moderately acidotic renal patient is much greater than the amount of acetate available in the initial dialysate. So Sorbent dialysis systems were designed to provide additional acetate. During dialysis, acetate continuously enters the dialysate from two sources.

The first source is the infusate. The SORB 10 Infusate is composed of calcium acetate and magnesium acetate. The infusate additives, K-1 and Ca-1/2, are also acetates. Each mEq of magnesium acetate, calcium acetate or potassium acetate added to the Cartridge effluent provides 1 mEq of acetate. Thus the amount of acetate that is added to each liter of regenerated dialysate depends on the composition of the infusate mixture. A basic SORB 10 Infusate will add 4 mEq of acetate to each liter of regenerated dialysate. Infusates containing K-1 and/or Ca-1/2 additives will add proportionately more acetate.

Since, at a dialysate flow rate of 200 ml/min, the Cartridge is processing 12 L of dialysate per hour, the infusate system adds 12 times 4 (or more) mEq of acetate to the reservoir every hour. Thus the patient is exposed to a minimum of 48 mEq of acetate each hour from this source, or at least 192 mEq during a 4 hour treatment. This figure would be 240 mEq/4 hour treatment for the REDY 2000 since, due to its dialysate flow rate of 250 ml/min, the dialysate turnover is 15 L/hr.

The second source of acetate is the Cartridge. Recall that the hydrated zirconium oxide layer of the Cartridge gives up 1 mEq of acetate in exchange for each mEq of phosphate that dialyzes out of the patient's body (as well as the phosphate and flouride in the tap water used to make the initial dialysate). An average contribution can be estimated to be about 100 mEq during a 4 hour treatment, assuming the post dialysis serum phosphate is about 2.5 mg/dl lower than the pre value and the patient's fluid volume is 42 L.

Thus during an entire 4 hour treatment the patient is exposed to about 500 mEq of acetate.

	DIALYSATE FLOW RATE	
	200 ml/min	250 ml/min
Initial Dialysate	210 mEq	210 mEq
Infusate (K=O)*	192 mEq	240 mEq
Cartridge	100 mEq	100 mEq
	502 mEq	550 mEq

Even so, this is only about one-eighth of the 4200 mEq of acetate available to the patient during a 4 hour single pass dialysis using an acetate dialysate. This difference in degree of acetate exposure has implications with respect to patient well-being which will be examined shortly. But prior to that, it is important to consider bicarbonate.

2.4.C Sources of Bicarbonate

There are two sources of bicarbonate in acetate dialysis: the patient and the Cartridge.

The initial dialysate contains no bicarbonate. Yet the patient, although acidotic, has bicarbonate in his body fluids. This difference in concentration causes bicarbonate to leave the patient and enter the used dialysate. Since the Cartridge does not adsorb appreciable quantities of bicarbonate in the presence of urea, most of the bicarbonate "lost" by the patient enters the reservoir. Due to the volume relationship between the patient and the dialysate (Section 2.1.C.), the patient's bicarbonate level will generally decrease 3 ± 1 mEq/L before he donates sufficient bicarbonate and urea to cause the dialysate to equilibrate with him.

The equilibrium phase is completed during the first hour of dialysis. Subsequently the bicarbonate level in the dialysate rises due to the contribution of the Cartridge.

The Cartridge generates some bicarbonate in exchange for adsorption of urea. Recall that the urease layer converts urea into ammonium carbonate. The ammonia is removed by the zirconium phosphate layer. In exchange for ammonia, zirconium phosphate releases a mixture of hydrogen and sodium ions. These ions combine with the carbonate, which is no longer attached to ammonium, to form carbonic acid (H_2CO_3) and sodium bicarbonate ($NaHCO_3$). Carbonic acid is unstable and quickly breaks down into CO_2 and water. The sodium and bicarbonate ions remain in the dialysate. An average of about 15% of the urea which enters the Cartridge is converted into sodium bicarbonate.

*Each K-1 additive packet will increase total acetate exposure by 48 mEq per 4 hour treatment at a 200 ml/min DFR or 50 mEq/4 hr (250 ml/min DFR). Each Ca-1/2 additive packet provides 24 mEq or 30 mEq, respectively, during a 4 hour treatment.

2.4.C Sources of Bicarbonate (continued)

An adult, of average body size, will cause the Cartridge to generate about 150 mEq of bicarbonate in this manner during a 4 hour dialysis.* Although this amount is not very large (due to the volume relationship, the patient regains about 3 mEq/L), it is sufficient to replace the bicarbonate "lost" from the patient to the reservoir at the start of the treatment.

NOTE: This discussion applies only to adults weighing more than 40 kg. See Section 2.6 (Special Considerations) for a discussion of dialysate prescription guidelines for small adult and pediatric patients.

2.4.D Patient Response to Mixed Acetate/Bicarbonate Dialysis

In order to understand the effects of acetate Sorbent dialysate on the patient, it is important to first review the patient response to single pass acetate dialysis.

During single pass dialysis, the patient is continuously exposed to dialysate which contains 35 mEq/L of acetate and no bicarbonate. As a result, the patient gains significant quantities of acetate and loses significant quantities of bicarbonate. The stable chronic dialysis patient (End Stage Renal Disease with no medical complications), is able to convert the acetate into bicarbonate rapidly enough to both correct his uremic acidosis and replace the bicarbonate lost during dialysis.

However, unstable chronic dialysis patients (ESRD with medical complications), acute dialysis patients and very elderly or very young dialysis patients are often unable to rapidly convert acetate into bicarbonate. As a result, one or both of the following conditions appear while the patient is on dialysis.

1. Increasing Acidosis: Unable to convert acetate rapidly enough to keep up with the continuous bicarbonate loss during single pass dialysis, the patient becomes increasingly acidotic while on the machine. Symptoms include weakness, restlessness, nausea and vomiting, and rapid deep respirations. The symptoms are most evident during the last hour of dialysis and usually resolve completely within 10 hours after dialysis, with or without treatment.

2. Acetate Intolerance: Acetate has a direct effect on the cardiovascular system, inducing both vasodilation and depression of myocardial contractility. Some patients are more sensitive to acetate than average while others, unable to rapidly convert acetate, develop unusually high blood levels of acetate before reacting to acetate directly. In either case the symptoms of vasodilation (headache, hypotension) and depressed myocardial contractility (decrease in heart rate, arrhythmias) characteristic of acetate intolerance develop during dialysis. Patients experiencing acetate intolerance consistently require more nursing intervention than is usual. In some cases, the symptoms are so severe the patient must be permanently switched to bicarbonate dialysate.

In recent years, the introduction of increasingly efficient dialyzers has resulted in decreases in total dialysis time. Unfortunately, with each decrease in dialysis time, some formerly stable patients destabilize. For instance, patients who could handle the acetate gain and bicarbonate loss efficiently during a 5 hour treatment, may develop symptoms of acidosis and/or acetate intolerance when asked to process the same amounts of acetate in a shorter period of time, such as 4 hours. Thus whenever dialysis time decreases, the proportion of patients who have problems with acetate increases.

Patients on Sorbent dialysis are protected from many of the problems associated with single pass acetate dialysis. As noted in the preceding section, they are exposed to neither as much acetate gain nor as much bicarbonate loss as occurs in an equivalent single pass treatment.

Since the closed dialysate pathway of Sorbent systems retains the patient's bicarbonate in the presence of urea, and the small volume of recirculating dialysate requires little bicarbonate transfer from the patient before the dialysate bicarbonate level is in equilibrium with the patient, the development of progressive acidosis (and its symptoms) is prevented.

Also, less total acetate transfer from dialysate to patient is required, since it is not necessary for the patient to receive acetate to replace bicarbonate lost during the dialysis. Thus serum acetate levels are not likely to rise to the point at which symptoms of acetate intolerance are triggered.

*This assumes the patient is uremic and thus presents significant quantities of urea to the cartridge (i.e., >10 grams).

2.5 BICARBONATE DIALYSATE

2.5.A. Standard Bicarbonate Bath

The standard bicarbonate bath was designed to provide enough bicarbonate to correct the degree of acidosis present in an uremic adult, i.e., to increase the patient's serum bicarbonate level by 4-9 mEq/L. The initial bath contains 30 mEq/L sodium bicarbonate. As with the situation with acetate dialysate, the initial amount of bicarbonate (or, in the case of acetate, bicarbonate precursor) is not enough to fully correct the acidosis; the remaining correction is provided by the bicarbonate generated by the sorbent cartridge as a byproduct of the breakdown of urea by the urease layer.

Bicarbonate dialysate is made with 6 L of water, using premeasured packets of chemicals, as is acetate dialysate. Unlike acetate dialysate, there are three different levels of bicarbonate dialysates, used to treat various degrees of acidosis. While bicarbonate dialysate is quickly made and easy to use, there are a few points to learn prior to performing bicarbonate dialysis with the sorbent dialysis system.

1. Bicarbonate dialysate must be neutralized prior to use.

Contrary to the situation with acetate in dialysate, bicarbonate dialysate is sightly alkaline (pH 8.2). Addition of calcium and magnesium infusate chemicals to this dialysate will cause their precipitation as carbonates, resulting in a milky white dialysate which will trigger false blood leak alarms. Thus the dialysate must be neutralized prior to adding the infusate (containing calcium and magnesium acetate) to the reservoir and placing the patient on dialysis.

Two methods are used to neutralize the dialysate. The acidifier (1N HCl) from the prescribed Bicarb Kit (available from COBE Renal Care) can be added to the dialysate and the infusate added thereafter, permitting patient dialysis to be initiated immediately. Alternatively an older method, commonly referred to as "cartridge titration" and established prior to the availability of Bicarb Kits, can be used. With this method the dialysate is passed through the cartridge for 15 minutes, during which time the zirconium phosphate (ZP) releases hydrogen ions in exchange for sodium ions obtained from the sodium bicarbonate.

Regardless of their source (acidifier or zirconium phosphate), the hydrogen ions combine with some of the bicarbonate converting it into carbon dioxide. This loss of bicarbonate combined with the formation of carbon dioxide causes the dialysate pH to decrease, resulting in a neutral dialysate to which the infusate can be added without causing a precipitate. The remaining bicarbonate (about half the original amount) is available to the patient.

It is necessary to provide extra bicarbonate in the REDY Chem bicarbonate dialysates in order to accommodate the neutralization reaction. For that reason the "standard" 30 mEq/L Bicarb 2 Kit contains 60 mEq/L when initially made: 30 mEq/L for the ZP layer and 30 mEq/L for the patient. It is the same for the other recommended bicarbonate dialysates.

2. The dialysate conductivity decreases until the patient is connected.

As the sodium from the dialysate is being adsorbed in exchange for hydrogen ions (see above), the sodium level in the dialysate progressively decreases. Since the majority of dialysate conductivity is due to the sodium level (see Section 2.3.B.), the conductivity progressively decreases.

Without the patient connected, the cartridge will continue to cause bicarbonate to change into carbon dioxide and to adsorb sodium until the dialysate composition is no longer desirable, i.e., is inadequate to correct the patient's chemistries. This point is reached within 30 minutes after the dialysate flow is first started through the cartridge. After 30 minutes the bicarbonate and sodium levels drop so low that a low level conductivity alarm is likely to occur and if a patient were to be connected, he would loose bicarbonate to the dialysate.

If, for some reason, the patient cannot be connected to the system during the initial 30 minute period, the machine must be put into CARTRIDGE BYPASS until dialysis can be started. The chemical levels in the dialysate do not change when the system is in CARTRIDGE BYPASS and the patient is not connected. (The machine can remain in CARTRIDGE BYPASS for a considerable period; however due to bacterial considerations it is recommended the dialysate be used within one hour. Past that time, the dialysate should be replaced with a fresh bicarbonate bath before the patient is connected.)

3. There are three bicarbonate dialysates.

Different patients have different degrees of acidosis. In sorbent dialysis the correction of acid-base problems involves an interaction between three potential sources of bicarbonate: the initial 6 liters of dialysate, the sorbent cartridge and the patient himself. (With sorbent acetate dialysis, only the patient

and cartridge are sources of bicarbonate, see Section 2.4.C.) Normally, the physician selects the appropriate bicarbonate dialysate from the table (see Table 2.3) on the basis of degree of serum bicarbonate correction desired. However, patients who are smaller than normal adult size, are not significantly uremic and/or are to be dialyzed for less than 3 hours will not trigger an adequate amount of additional bicarbonate production from the cartridge to complete the correction of their acidosis. The physician then selects one of the methods for compensating for this (see Section 2.7, Special Considerations).

Since the patient does not loose any of his body bicarbonate during the treatment and the amount of bicarbonate generated by the cartridge is fixed in relation to the patient's body size and degree of uremia, the reservoir is the place where the amount of bicarbonate (i.e., total dose) presented to the patient can most easily be varied. The amount of bicarbonate in the dialysate does not have to be very large because nothing goes down the drain and the cartridge continuously adds additional bicarbonate. So for example when a patient is mildly acidotic, a 10 mEq/L initial bicarbonate dialysate is adequate in a sorbent system, even though that would be unsafe in a single pass dialysis system. Conversely, if a patient has severe acidosis and needs a lot of bicarbonate, the small 6 liter bath will need a lot of bicarbonate in it in order to transfer a sufficient amount to the patient. That is why the dialysate for severe acidosis contains 50 mEq/L—an amount that could be dangerous in a single pass system. Most patients are moderately acidotic and require the standard bicarbonate dialysate, which contains 30 mEq/L.

Note: Some dialysis patients are not acidotic; they may have normal acid-base status or they may even be alkalotic. There are special dialysates for these patients—see *The Guide to Custom Dialysis*, Chapter 1, for more information.

Table 2.3: Dialysates to Adjust the Blood Bicarbonate

Patient's Status	Desired Increase in Serum Bicarbonate (mEq/L)	DIALYSATE Sodium Bicarbonate (mmol/L)	Sodium Chloride (mmol/L)	Initial Dialysate Conductivity (mMho)
Severe Acidosis	>10	100	40	11.4
Moderate Acidosis	4-9	60	80	13.4
Mild Acidosis or Normal Acid-Base	2-4	20	120	14.0

4. There is acetate in the bicarbonate dialysate.

A small amount of acetate is unavoidable. The acetate comes from two sources. The infusate chemicals are acetates (calcium acetate, magnesium acetate and potassium acetate) and, depending on the amount of potassium prescribed, infusate contributes between 4-8 mEq/L of acetate to the dialysate in the reservoir. Also, the hydrated zirconium oxide layer contributes a small amount of acetate to the regenerated dialysate in exchange for removing phosphate from the used dialysate. The total amount of acetate is approximately the same as that found in single pass bicarbonate dialysates, which use acetic acid to stabilize the pH of the "acid" concentrate. In both cases, this small amount of acetate is readily converted into bicarbonate even by the sickest patients and thus is an additional help in correcting their acidosis.

5. Dextrose should be added to bicarbonate dialysate.

It is recommended that 48 grams of dextrose be added to the intitial dialysate in order to maintain plasma osmolality (the glucose moves into the patient's plasma as uremic toxins are being removed). This will not only minimize disequilibrium symptoms (for example, headache and restlessness) and assist in maintaining blood pressure, but will also help avoid hypoglycemia in the diabetic or malnourished patient whose glycogen stores are depleted.

The 48 grams of dextrose added to the 6 L bicarbonate dialysate provides for the same dextrose transfer as dialyzing against a 200 mg/dl dextrose single pass dialysate. The average diabetic (and non-diabetic) patient does not require a change in insulin dosage with this amount of dextrose exposure since the sorbent cartridge is constantly regulating the dextrose level in the dialysate (see Glucose in Section 2.2).

2.5.B. Sources of Bicarbonate

There are three sources of bicarbonate in the sorbent system during bicarbonate dialysis: the initial dialysate, the cartridge and the patient. As discussed in the preceding section (2.5.A.3.), the patient is not a significant source. The amount of bicarbonate generated by the cartridge during the treatment is determined by the amount of urea the patient presents to the urease layer; this, in turn, is determined by the patient's predialysis SUN and body size. Because the amount of bicarbonate in the initial dialysate takes into account the bicarbonate expected from the cartridge during dialysis of a uremic adult, patients who are not uremic or are not adults—but are acidotic—will only be properly corrected if the initial bath is adjusted for these differences (see Special Considerations, Section 2.7).

2.6 CARBON DIOXIDE

2.6.A. Sources of Carbon Dioxide

Carbon dioxide enters the dialysate early in the dialysis as the patient "donates" carbon dioxide and bicarbonate (some of which breaks down into carbon dioxide and water) to the dialysate until equilibrium occurs. Subsequently carbon dioxide is produced in the Sorbent Cartridge in exhange for ammonia adsorption. As one of the components of Cartridge effluent, carbon dioxide is returned to the reservoir as part of the regenerated dialysate.

Most of the carbon dioxide escapes into the atmosphere (Figure 2.4). However some of the carbon dioxide (CO_2) remains dissolved in the dialysate, where it serves to stabilize the pH. Among other things, maintenance of proper dialysate pH prevents the calcium in dialysate from turning into calcium carbonate (lime), a precipitate which turns the bath milky white.

As the CO_2 dissolved in the dialysate enters the dialyzer, some of it crosses the membrane into the patient's blood. There it joins the CO_2 already in the patient's blood as a result of normal cell metabolism. Carbon dioxide is eventually carried to the lungs, where it is expired.

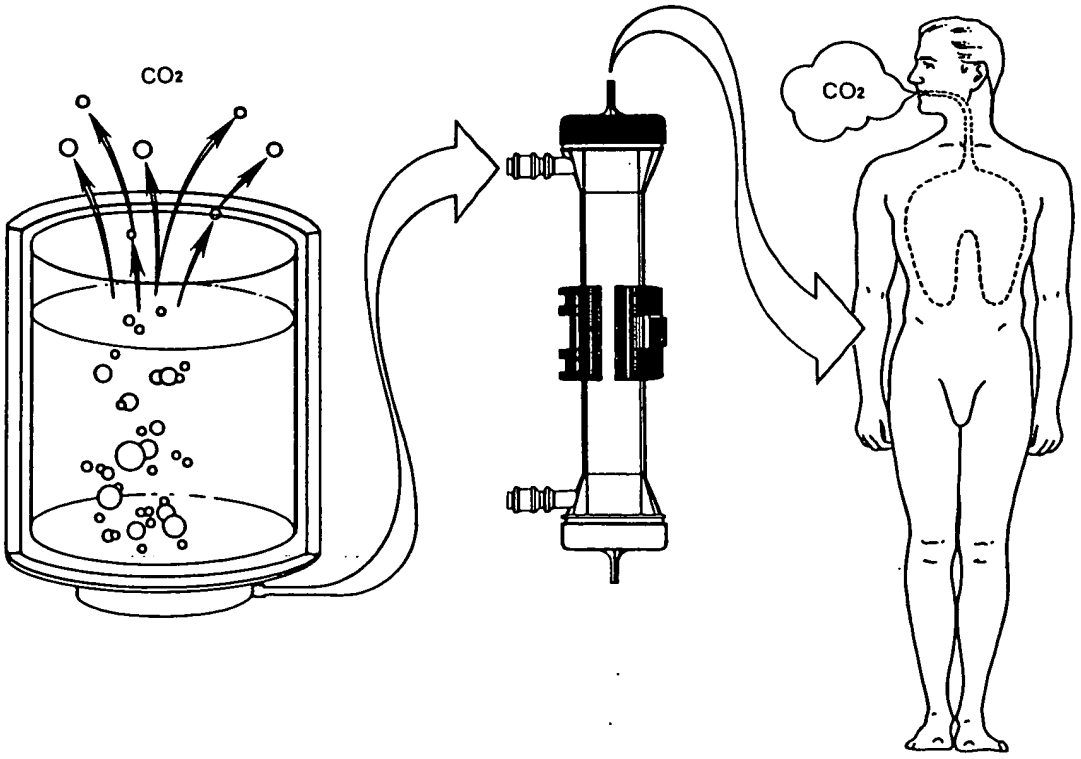


Figure 2.4: Dialysate CO_2 Disposition

*Avoid adding sodium bicarbonate to the initial dialysate. The cartridge will remove about 50% of bicarbonate present during the initial prime of the dialysate pathway. Once the patient is connected, the presence of even minimal urea in the system will avert significant reduction of dialysate bicarbonate.

2.6.B. Effects of Carbon Dioxide

With sorbent dialysis the patient loses carbon dioxide to the dialysate only during the first 30-60 minutes of the treatment and receives carbon dioxide from the bath for the rest of the procedure. For this reason, the blood in the venous line will have a higher CO_2 content (and thus be slightly darker in color) than during single pass dialysis.

In single pass acetate dialysis the patient loses CO_2 continuously throughout the treatment. The resulting decrease in blood CO_2 depresses the respiratory rate, which causes a variable degree of hypoxia (sometimes severe). Dialysis-induced hypoxia can be a grave complication for certain patients; for example, those with a concurrent respiratory disorder or unusually severe anemia. Dialysis-induced hypoxia is prevented by Sorbent acetate dialysis because there is no CO_2 loss—in fact the patient gains a little. However, the amount of CO_2 gained is so small, compared to the metabolic CO_2 already present in the patient's blood, that it causes no change in respiratory rate.

In addition to darker blood in the venous line, the higher CO_2 content of Sorbent dialysate is visible in another way: as gas bubbles in the dialyzer and dialysate lines. The dissolved CO_2 will come out of the solution, i.e., "degas", primarily as a result of vacuum (negative pressure) being applied to the dialysate. The higher the negative pressure, the more CO_2 will degas.

At moderate to high negative pressures (250 mmHg and above), the amount of CO_2 being degassed from the dialysate can result in a steady stream of large CO_2 bubbles visible in the "to dialyzer" dialysate line and in an accumulation of gas in the dialysate compartment of the dialyzer. Although very little membrane surface is masked (i.e., dialysate is prevented from reaching it) by the accumulated gas, most operators prefer not to have the gas present in the dialysate. The bubbles can be removed from the dialyzer by periodically (ex., every 30 minutes) putting the machine into Cartridge Bypass for 4 or 5 seconds.* Without the Cartridge in the circuit, the dialysate flow rate increases to 600-700 ml/min; the force of this flow "washes" the CO_2 bubbles away. (Some people call this procedure "burping the dialyzer".) CAUTION: DO NOT LEAVE THE MACHINE IN CARTRIDGE BYPASS. When the Cartridge is bypassed, used dialysate is not being regenerated. Ultrafiltration continues but little biochemical exchange occurs after a few minutes in bypass, since the dialysate will equilibrate with the patient.

An easier alternative is to minimize the accumulation of CO_2 bubbles. This can be accomplished in two ways. It is most effective if both are used together.

1. TILT THE DIALYZER AT A 45° ANGLE (Figure 2.5). This places the dialysate exit port at the top of the dialyzer. Since gas always rises in a solution, the bubbles will move through and immediately out of the dialyzer.
2. SPLIT THE TRANSMEMBRANE PRESSURE. Splitting the required TMP results in a negative pressure below 250 mmHg, thus reducing the amount of CO_2 that is degassed. If, for example, the patient requires a TMP of 400 mmHg for ultrafiltration, apply half as negative dialysate pressure and the rest as positive (i.e., venous) blood pressure. In this example, a screw clamp (also called a "C" clamp) would be used to increase the venous pressure from that of the patient's venous resistance to +200 mmHg (Figure 2.6).

   For the REDY 2000: If unacceptable levels of CO_2 bubbles appear, it will most likely be after the UF Control system has stabilized at the optimal TMP for the requested fluid loss. Note that TMP level, then

*The REDY 2000 does this automatically every 6-7 minutes.

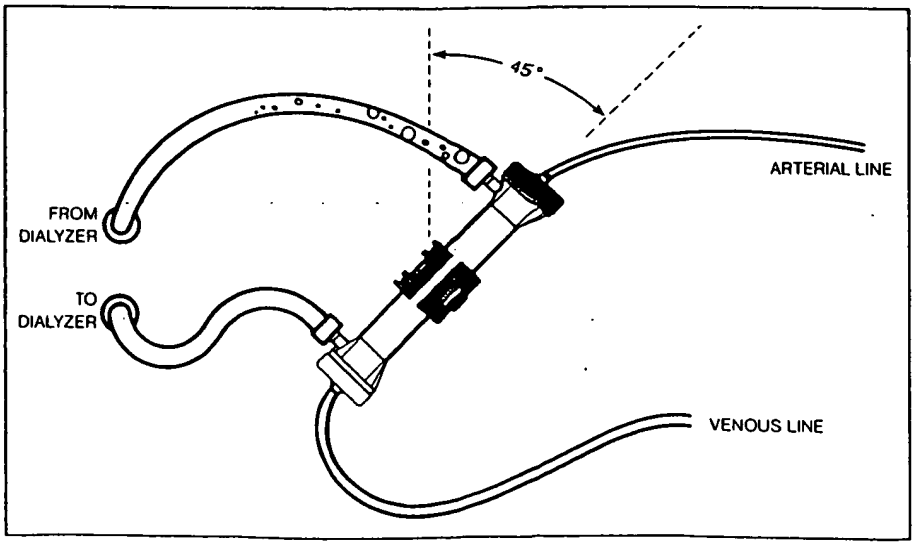


Figure 2.5: Degassing the Dialyzer

2.6.B Effects of Carbon Dioxide (continued)

use the venous resistance knob provided on the lower left corner of the front panel to increase the venous pressure to a value equal to one-half the displayed TMP. As the venous resistance increases, the REDY 2000 will automatically reduce the negative pressure in order to maintain the optimal TMP.

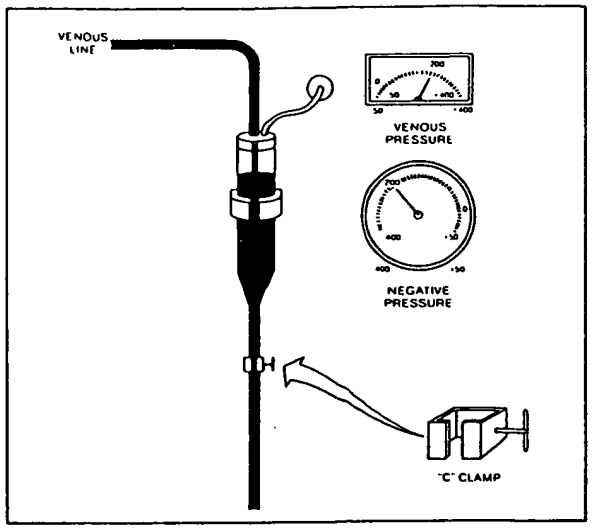


Figure 2.6: Divided TMP

2.7 SPECIAL CONSIDERATIONS

2.7.A. Short Treatment Time

In the prior sections of this booklet, the discussion has addressed the changes to dialysate and to the patient during a 4 hour sorbent dialysis treatment. When dialysis times are reduced to 2 or 3 hours, there are several issues which must be considered.

UREA REDUCTION: The usual treatment goal is a reduction in pre dialysis serum urea of at least 50%. If a similar reduction is desired for a short time dialysis treatment, appropriate dialyzer selection is imperative. Consideration should be given to selection of a dialyzer with a higher urea clearance value than was required for the same patient undergoing a 4 hour treatment.

SODIUM: When the initial dialysate sodium level is 120 mEq/L, the normonatremic patient will donate sodium to the bath until equilbrium occurs (approximately 45 minutes into the treatment). The patient will gradually regain the donated sodium and return to his pre dialysis serum sodium level by the end of 4 hours. However when dialysis time is shortened to 2 to 3 hours, the normonatremic patient will probably not have sufficient time to recover his donated sodium. Thus, short time dialysis should begin with an initial dialysate sodium of 130 to 135 mEq/L (approximately 175 ml liquid acetate concentrate in 6L water.)

If the patient is hyponatremic or hypernatremic pre dialysis, follow the directions in section 2.3.C., Manipulation of Patient Sodium.

ACID-BASE BALANCE: Correction of acidosis during short time dialysis may necessitate bicarbonate supplementation similar to that required by small or non-uremic patients, particularly if the short time patient is severly acidotic pre dialysis. It is recommended that the guidelines in Section 2.7.B. be applied to uremic adults undergoing short time dialysis.

2.7.B. Non-Uremic Patients

Occasionally it is necessary to dialyze a patient who is not uremic. Such patients represent a special subgroup in sorbent dialysis. When the patient cannot provide sufficient urea (at least ten grams, presented to the cartridge over a 3-4 hour period), the cartridge cannot produce enough CO_2 and bicarbonate to increase dialysate pH and bicarbonate levels. Thus acidosis will not be corrected and, in rare instances, may worsen. For this reason, patients who cannot present sufficient urea to the cartridge should receive supplemental bicarbonate during sorbent dialysis. This can be provided by periodic addition of sodium bicarbonate to the dialysate (five grams of $NaHCO_3$ will raise the bicarbonate concentration by 10 mEq/L) or to the patient, via administration of parenteral bicarbonate solutions into the venous blood line. Blood pH and bicarbonate levels, drawn periodically (but definitely 90 minutes prior to the end of dialysis), can be used as a guide for bicarbonate supplementation.

2.7.C. Pediatric and Small Adult Patients

As body fluid volume more closely approaches the volume of the dialysate in the reservoir, the biochemical relationship between the patient and dialysate more closely approximates that of single pass dialysis. This does not affect ultrafiltration, the removal of uremic toxins, or correction of potassium, calcium or magnesium imbalances but has some implications with respect to sodium and bicarbonate.

1. Sodium

If the patient is normonatremic, dialysate sodium should be maintained at 135-140 mEq/L throughout the dialysis by controlling dialysate conductivity using the methods described in section 2.3.C. of this Primer.

2. Bicarbonate

Small uremic patients may not transfer enough urea for the sorbent cartridge to generate adequate bicarbonate to correct their acidosis, particularly if the acidosis is severe. For this reason, it may be necessary to select a dialysate providing more bicarbonate than that indicated in Table 2.3 (Dialysates to Adjust the Blood Bicarbonate) for the patient's degree of acidosis. Alternatively, during the dialysis, bicarbonate can be added to the reservoir or parenterally via the venous bloodline. Each gram of $NaHCO_3$ added to the reservoir during dialysis will raise the dialysate bicarbonate concentration by 2 mEq/L. It is recommended that blood gases be monitored as a guide to supplementation.

DIALYSATE PURIFICATION

3.1 WATER QUALITY DETERMINATION

As water quality in various parts of the world continues to deteriorate and water quality standards for hemodialysis become more narrowly defined, it may be necessary in some circumstances to pretreat the water used even in sorbent dialysis systems.

Whether pretreatment should be done for a given dialysis depends upon the quality of the tap water available for dialysis and the water quality philosophy adopted by the unit. For example, a different set of standards might be used for acute (temporary) and chronic (permanent) patients.

The following tables are provided to assist in the preparation of dialysate which meets AAMI/ANSI* standards.

The results of routine periodic analysis of available tap water are necessary in order to use the tables. It is suggested that serial analyses be done as water quality in a given area tends to vary considerably over time. It is not necessary to analyze water for all the chemicals listed (the local water district can supply some of the data on a periodic basis, probably free of charge) but items of special interest, such as chloramines, calcium, aluminum, etc., may need to be monitored separately by the dialysis unit.

To use the tables (Table 3.1 below), identify the chemical elements of special interest, locate the column that most closely approximates their levels in your tap water and follow the listed recommendations.

Recommendation:

1. If chemical levels are equal to or lower than those listed in the maximum for "STANDARD REDY PREP" column, below, no treatment is necessary. The 15-20 minute recirculation of dialysate which occurs during the standard recommended set-up procedure is adequate to purify dialysate.
2. If chemical levels exceed the maximum for "STANDARD REDY PREP" but are lower than in the maximum for "REDY PURIFICATION" column, use one of the dialysate purification procedures on pages 32-34.
3. If chemical levels exceed the maximum for "REDY PURIFICATION" column, use purified water (for example, distilled, reverse osmosis or deionized) to make dialysate.

Table 3.1: Water Quality

WATER QUALITY CHART

	AAMI/ANSI[1]	REQUIRES STANDARD REDY PREP		REQUIRES REDY PURIFICATION		REQUIRES PURIFIED WATER
		MAXIMUM		MAXIMUM		
SUBSTANCE	mEq/L mg/L	mEq/L	mg/L	mEq/L	mg/L	
Aluminum	0.01		0.03		1.0	
Arsenic	0.005		0.015		0.05	
Barium	0.1		0.3		1.0	
Calcium[2]	0.1 2.0	4.5	90.0	7.2	145.0	
Cadmium	0.001		0.003		0.01	
Chlorine	0.5		1.5		6.0	
Chloramines	0.1		0.3		6.0	
Chromium	0.014		0.042		0.7	
Copper	0.1		0.3		0.5	
Fluoride	0.2		0.6		2.0	
Lead	0.005		0.015		0.05	
Magnesium[2]	0.3 4.0	2.0	24.0	3.3	40.0	
Mercury	0.0002		0.0006		0.002	
Nitrate	2.0		2.0		2.0	
Postassium[2]	0.2 8.0	0.5	20.0	1.5	60.0	
Selenium	0.09		0.27		0.9	
Silver	0.005		0.015		0.05	
Sodium[3]	3.0 70.0	3.0	70.0	3.0	70.0	
Sulfate	100.0		100.0		100.0	
Zinc	0.1		0.3		1.0	
Bacteria	200/ml		600/ml		2000/ml	

[1]Based on the AAMI/ANSI Guidelines for water used to make hemodialysate, March, 1992.
[2]Sorbent Cartridges completely remove these substances. They are then replaced at the desired level by the infusate system.
[3]The volume of concentrate added to the six liters of water should be adjusted to compensate for the presence of sodium in tap water.

*Association for the Advancement of Medical Instrumentation/American National Standards Institute, Inc.

3.2 CHLORAMINE REMOVAL

Rapid Dialysate Purification – Chloramine Removal Only

1. Prepare dialysate using six liters of warm water in jug provided with machine.
2. Add Ascorbic Acid (see note) to dialysate mixture in six liter jug; one Ascorbic Acid packet is sufficient to remove up to 10 mg/L of chloramines from 6 L of dialysate. Swirl fluid in jug briefly to mix.
3. Continue set-up procedure as usual.

NOTE: The premeasured Ascorbic Acid (180 mg) is packaged with a small amount of dextrose (4 gm) which serves as a blending agent. The amount of dextrose in the final six liters of dialysate is negligible (67 mg/dl) and will neither harm nor benefit the patient.

3.3 DIALYSATE PURIFICATION METHODS

3.3.A. Dialysate Purification – Acetate Dialysate

Purpose: To remove aluminum, chloramines, and other undesirable substances from acetate dialysate made with potable tap water which exceeds REDY standards but is lower than REDY Purification Level (Table 3.1).

Note: DO NOT use this procedure to purify tap water. Sorbent Cartridges were not designed to handle plain water; damage to the contents of the cartridge may result. Use this procedure on acetate and chloride dialysates only.

Extra Materials Needed: Purification Adaptor, which consists of 3 feet of 0.2" X 0.1" I.D. silastic tubing attached to a cartridge connector. Purification Adaptor can be obtained by contacting COBE Renal Care.

Procedure:

1. Prepare dialysate in 6 L jug provided with the REDY (Note).
2. Place cartridge and infusate on machine as usual.
3. Turn power ON. Sequence system to "SYSTEM READY". Add dialysate to reservoir. Place 6 L jug next to machine.
4. In place of usual connector at top of cartridge, insert the Purification Adaptor with open end of tubing going into 6 L jug. (Fig. 3.1, page 33.)
5. Press STANDBY: system will go into its priming sequence.
6. Meanwhile, set-up dialyzer and blood lines: perform saline prime as usual.
7. Collect purified cartridge effluent in 6 L jug until reservoir is low. Reservoir will not completely empty: jug will contain about 4 L of fluid.
8. Drain unprocessed fluid from reservoir: turn power OFF.
9. Restart system and pour purified dialysate accumulated in jug into machine reservoir.
10. Add 10 ml of infusate to reservoir to provide prescribed amount of calcium, magnesium, and potassium.
11. Remove Purification connector from top of cartridge and replace with cartridge connector on REDY SYSTEM.
12. Connect dialysate lines to dialyzer.
13. Press STANDBY.
14. System is ready for dialysis.

3.3.B. Dialysate Purification: Bicarbonate Dialysate

CARTRIDGE TITRATION

General Method:
Sorbent bicarbonate dialysate "concentrate" consists of two chemicals, NaCl and $NaHCO_3$. The bicarbonate purification procedure involves purifying a mixture of NaCl in six liters of water first, then adding the $NaHCO_3$. The NaCl must be added to the water because plain tap water will damage the cartridge. The $NaHCO_3$ must be added after the purification is accomplished because too much of it will be coverted into CO_2 gas—and lost to the atmosphere—if it is "single passed" through the cartridge with the NaCl and water.

Extra Material Needed:
Purification Adaptor, which consists of a cartridge connector with 3 feet ¼" O.D. PVC tubing attached. These materials can be purchased from COBE Renal Care.

Procedure:

1. Mix the prescribed amount of NaCl with 6 liters warm water in the jug provided with the REDY® system.
2. Fill the infusate jar with water and connect to the machine. Place cartridge on machine but replace usual connector at top of cartridge with the purification adaptor.
3. Turn power ON. Pour contents of jug into reservoir and place empty jug next to machine. Put open end of purification adaptor tubing into jug. (Fig. 3.1)
4. Press STANDBY. System will begin priming.
5. Set up dialyzer and blood lines; perform saline prime as usual. Mix prescribed infusate and set aside.
6. Collect purified cartridge effluent in 6-liter jug until at least 4 liters have been collected, then drain any unprocessed dialysate from reservoir and turn power OFF.
7. Remove purification adaptor from top of cartridge and replace with cartridge connector on REDY® system.
8. Add prescribed amount of $NaHCO_3$ and dextrose to fluid in 6-liter jug. Swirl contents to mix.
9. Restart system and pour contents of jug into machine reservoir.
10. Allow dialysate to recirculate for 15 minutes.
11. At the end of recirculation period, connect prescribed infusate to the infusate system in place of water. Add 10 ml of infusate to reservoir to provide prescribed amounts of calcium, magnesium, and potassium to initial dialysate.
12. Activate DIALYZER BYPASS, connect dialysate lines to dialyzer, deactivate DIALYZER BYPASS. System is ready for dialysis. (See NOTE)

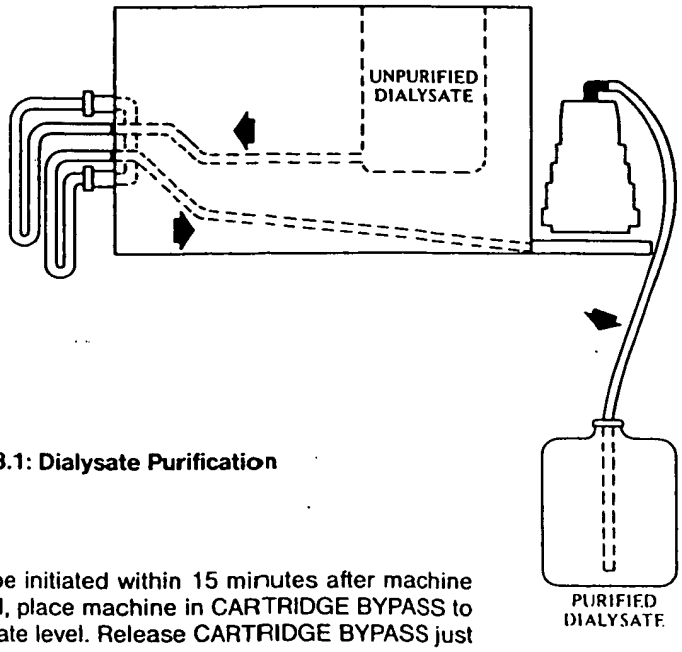


Figure 3.1: Dialysate Purification

NOTE: If dialysis cannot be initiated within 15 minutes after machine setup is completed, place machine in CARTRIDGE BYPASS to preserve bicarbonate level. Release CARTRIDGE BYPASS just before the patient is connected.

BICARB KITS

General Method:
Sorbent bicarbonate dialysate "concentrate" consists of two chemicals, NaCl and $NaHCO_3$. The bicarbonate purification procedure involves purifying a mixture of NaCl in six liters of water first, then adding the $NaHCO_3$. The NaCl must be added to the water because plain tap water will damage the cartridge. The $NaHCO_3$ must be added after the purification is accomplished because too much of it will be coverted into CO_2 gas – and lost to the atmosphere – if it is "single passed" through the cartridge with the NaCl and water.

Extra Materials Needed:
Purification Adaptor, which consists of a cartridge connector with 3 feet ¼" O.D. PVC tubing attached. These materials can be purchased from COBE Renal Care.

Procedure:

1. Mix the prescribed amount of NaCl with 6 liters warm water in the jug provided with the REDY® system.
2. Place cartridge and infusate on machine as usual. In place of usual connector at top of cartridge, insert the purification adaptor.
3. Turn power ON. Pour contents of jug into reservoir and place empty jug next to machine. Put open end of purification adaptor tubing into jug. (See Fig. 3.1, page 33.)
4. Press STANDBY. System will begin priming.
5. Set up dialyzer and blood lines; perform saline prime as usual.
6. Collect purified cartridge effluent in 6-liter jug until jug contains at least 4.0 liters of fluid, then drain any unprocessed fluid from reservoir and turn power off.
7. Remove purification adaptor from top of cartridge and replace with cartridge connector on REDY® system.
8. Add prescribed amounts of $NaHCO_3$, dextrose and acid to fluid accumulated in jug, swirl contents to mix.
9. Restart system and pour contents of jug into machine reservoir.
10. Add 10 ml of infusate to reservoir to provide prescribed amount of calcium, magnesium, and potassium. Stir briefly with any clean plastic implement to mix.
11. Activate DIALYZER BYPASS, connect dialysate lines to dialyzer, press STANDBY to deactivate bypass. System is ready for dialysis. (See NOTE, page 33.)

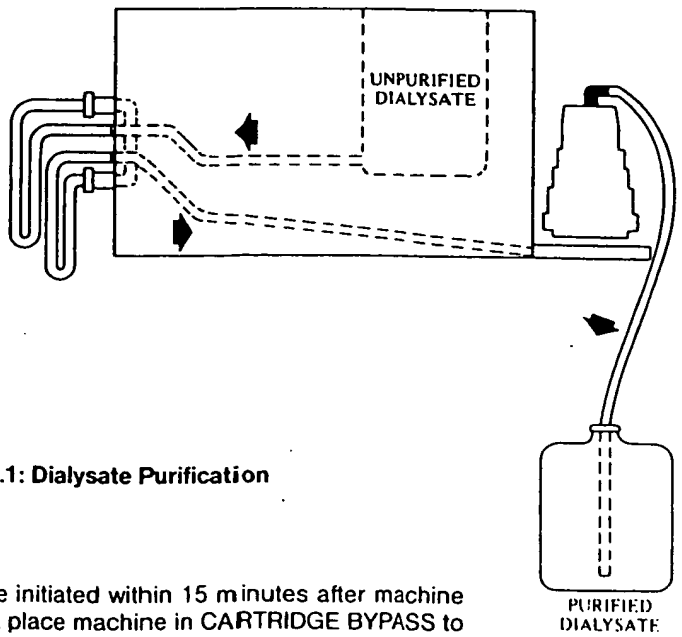


Figure 3.1: Dialysate Purification

NOTE: If dialysis cannot be initiated within 15 minutes after machine setup is completed, place machine in CARTRIDGE BYPASS to preserve bicarbonate level. Release CARTRIDGE BYPASS just before the patient is connected.

MACHINE DISINFECTION

4.1 BASIC INFORMATION

Patients with chronic and acute conditions requiring hemodialysis are susceptible to various infectious diseases which can be spread to other patients or staff members. Accordingly, various measures should be undertaken to prevent cross-infection, one of importance being the internal and external disinfection of dialysis machines.

The procedures in this Chapter were developed by Organon Teknika specifically for the Sorbent dialysis systems (REDY, SORBSYSTEM, REDY 2000) in consultation with the Centers for Disease Control and Prevention, Atlanta, Georgia.

When considering disinfection procedures for dialysis equipment, specifically Sorbent dialysis systems, it is recommended that the following information be kept in mind.

Effectiveness of Disinfectants
When used according to the instructions in this Chapter, formaldehyde, peracetic acid (Actril®) and sodium hypochlorite (bleach) are equally effective in disinfecting Sorbent dialysis systems.

Importance of Time:Concentration Ratio
There is an inverse relationship between the concentration of any given disinfectant and the time it is in contact with an item before adequate disinfection occurs. For example, if the concentration of a disinfectant is decreased (diluted), the time it is left in a dialysis machine must be increased.

Formaldehyde (2%) solution requires a dwell time of many hours. The 1200 ppm free chlorine bleach and Actril® solutions recommended in this chapter are effective in a matter of minutes and, in fact, **may damage the equipment** if repeatedly left in contact with machines for 30 minutes or longer.

The time:concentration ratios presented in this chapter were selected because they conform to procedures currently considered to be effective against the microorganisms commonly of concern to nephrology centers, including Hepatitis B and AIDS associated virus (HIV).

Since it is impossible to completely drain dialysis machines and microorganisms will multiply in standing water, disinfectants should not be rinsed from machines until immediately prior to dialysis. **This means the bleach and Actril® procedures should always be performed immediately prior to dialysis.** Reference: Alter MJ, Favero MS, Moyer LA, Miller JK, Bland LA; "National Surveillance of Dialysis-Associated Diseases in the United States, 1988." *Trans ASAIO* 36: 107-118, 1990.

Effectiveness of Recommended Methods
The routine internal and external machine disinfection methods recommended in this Chapter meet current recommendations for effective disinfection. In the absence of a blood-to-dialysate leak, no additional measures are required after dialyzing a patient suspected of having AIDS or Hepatitis B.

Removal of Machine from Isolation Areas
In the absence of a blood-to-dialysate leak, no additional measures are necessary before returning a machine to general use if routine disinfection has been performed according to the recommended procedures.

Special Disinfection
Special internal disinfection methods[1] are required ONLY if there has been a blood-to-dialysate leak while dialyzing a patient who is:

a) known or suspected to be antigen positive for Hepatitis B virus or antibody positive for HIV virus.
b) known to have an active case of AIDS or Hepatitis B (persons in the late stages of these diseases may be antigen negative.)

Machine Cultures
Cultures should be obtained just as the last water rinse of the disinfection procedure is being completed.

It is recommended that cultures be taken of the rinse fluid coming out of the cartridge effluent port (see Figure 1.5), on the basis that this fluid has been through both the entire dialysate circuit, and thus should have picked up microorganisms if they are present in any portion of the dialysate pathway. Other sites which may be cultured are (1) bottom of the reservoir, and (2) inside the dialysate line leading to the dialyzer.

If the dialysate lines are used as a culture site, the culture should be obtained as a clean catch specimen shortly after the Hansen connectors have been disinfected, in order to avoid secondary contamination of the specimen. Hansen connectors should be disinfected on a regular basis—once a month is recommended for machines that are used 5-6 days per week. [Hansen connectors may be disinfected by soaking in a 0.1% bleach solution (1 part 5.25-6.0% sodium hypochlorite to 49 parts water) for one hour, then thoroughly rinsed in AAMI standard (<200 CFUs/ml) tap water.]

[1] See Section 4.4, this Chapter

4.1 BASIC INFORMATION (continued)

Dialysate Disinfection

Dialysate may contain microorganisms. The Sorbent Cartridge is an excellent bacterial filter. As dialysate circulates through the Cartridge during dialysis, this filtration process keeps the microbial population and bacterial endotoxin levels within acceptable limits.[1]

If there is reason to suspect the water used to make the initial dialysate may be significantly contaminated (600-2000 microorganisms per ml) the Dialysate Purification Procedure appropriate for the machine model and dialysate type (acetate or bicarbonate) can be used to remove microorganisms[2]. Water obtained by reverse osmosis (RO) or commercially bottled water (i.e., from the supermarket) should be used if tap water is massively contaminated with bacteria, (i.e., greater than 2,000 microorganisms per milliliter).

The operator should note that failure to disinfect the 6 liter jug prior to each use can also result in contamination of the initial dialysate.

[1]Reference: Petersen, N.J., et al, "Removal of Bacteria and Bacterial Endotoxin from Dialysis Fluids by Sorbents", *ASAIO Journal*, Volume 3, number 1, pages 6-10, 1980.

[2]See Dialysate Purification Procedures, Section 4, *Guide to Custom Dialysis* or Section 3, *Sorbent Dialysis Primer.*

4.2 ROUTINE DISINFECTION

4.2.A. Bleach Procedure—Routine Disinfection

When to use this procedure:
—**Before every** dialysis (unless another disinfection procedure has been substituted)
—Post dialysis, if a blood leak has occurred
—Post dialysis, if machine is not to be used within 48 hours (72 hours, for home dialysis machines)

PROCEDURE	COMMENTS
AFTER EACH TREATMENT:	
1. Drain dialysate from machine.	
2. Add at least 3 liters tap water to reservoir. Circulate water through system for 2-3 minutes. Drain machine.	Water rinse physically reduces bacterial count.
3. Remove blood and dialysate spills, if any, from exterior of machine and cart.	Crusted material can serve as a site of microorganism colonization. Disinfectants may not penetrate crusted material.
4. Using disinfectant, wipe down exterior of machine, dialysate and electrical lines, cart and jugs. NOTE: Machine may be stored up to 48 hours after steps 1-4 have been completed.	Pay special attention to frequently touched areas, such as control knobs. Use a 700 ppm free chlorine solution (¼ cup 5.25% bleach added to 1 gallon tap water; make fresh daily).
PRIOR TO NEXT TREATMENT:	
5. Circulate a 1200 ppm free chlorine (bleach) solution through machine and infusate system.	See machine Operator's Manual for specific steps of bleach procedure. Infusate system disinfection procedure is in section 4.3 of this primer. To make 1200 ppm free chlorine solution, add 150 ml 5.25% bleach to 6 liters tap water.
6. Rinse machine at least twice with water; perform residual bleach test.	Obtain specimen for residual test from last water exiting drain hose after final water rinse. Use a currently acceptable residual bleach test.*
7. Six liter jug (plus 10 liter RINSE jug with REDY 2000) should be disinfected with bleach prior to each use.	Use same bleach solution, contact time and rinse procedure as used for equipment disinfection. It is unnecessary to disinfect the drain jug since its contents do not come into contact with the dialysate pathway.

*Examples: Hemastix (Ames laboratories), potassium iodide starch strips (Fischer Scientific).

4.2.B. Peracetic Acid (Actril)* — Routine Disinfection

When to use this procedure:
— **Before every** dialysis (unless another disinfection procedure has been substituted)
— Post dialysis, if a blood leak has occurred
— Post dialysis, if machine is not be be used within 48 hours (72 hours, for home dialysis machines)

PROCEDURE	COMMENTS
AFTER EACH TREATMENT:	
1. Drain dialysate from machine.	
2. Add at least 3 liters tap water to reservoir. Circulate water through system for 2-3 minutes. Drain machine.	Water rinse physically reduces bacterial count.
3. Remove blood and dialysate spills, if any, from exterior of machine and cart.	Crusted material can serve as a site of micro-organism colonization. Disinfectants may not penetrate crusted material.
4. Using disinfectant, wipe down exterior of machine, dialysate and electrical lines, cart and jugs. NOTE: Machine may be stored up to 48 hours after steps 1-4 have been completed.	Pay special attention to frequently touched areas, such as control knobs. Use 700 ppm free chlorine solution (¼ cup 5.25% bleach added to 1 gallon tap water; make fresh daily).
PRIOR TO NEXT TREATMENT:	
5. Circulate peracetic acid solution throughout machine and infusate system for 30 minutes. (Use MANUAL CLEAN mode on REDY 2000).	To make 34:1 peracetic acid solution, add 90 ml Actril to 3 liters tap water. NOTE: DO NOT USE RENALIN, AS THIS STRONGER FORM OF PERACETIC ACID IS CAUSTIC TO CERTAIN MACHINE COMPONENTS. Infusate system disinfection procedure is in section 4.3 of this primer.
6. Rinse machine at least twice with water; perform residual peracetic acid test.	Obtain specimen for residual test from last water exiting drain hose after final water rinse. Use residual test recommended by manufacturer of Acrtil.
7. Six liter jug (plus 10 liter RINSE jug with REDY 2000) should be disinfected prior to each treatment.	Use same disinfectant solution, contact time and water rinse procedure as used for equipment disinfection. It is unnecessary to disinfect the drain jug since its contents do not come into contact with the dialysate pathway.

*Registered Trademark, Renal Systems, Division of Minntech Corp., Minneapolis, MN.

4.2.C. Formaldehyde Procedure

When to use this procedure:
– Between treatments
(NOTE: This is a minimum 12 hour procedure, thus it is not suitable for use between two treatments scheduled for the same day.)
– Post dialysis, if machine is to be stored for up to one month.

PROCEDURE	COMMENTS
AFTER TREATMENT:	
1. Drain dialysate from machine.	
2. Remove blood and dialysate spills, if any, from exterior of machine and cart.	Crusted material can serve as a site of micro-organism colonization. Disinfectants may not penetrate crusted material.
3. Using bleach (free chlorine solution), wipe down exterior of machine, dialysate and electrical lines, cart and jugs.	Pay special attention to frequently touched areas, such as control knobs. Use a 700 ppm free chlorine solution (¼ cup 5.25% bleach added to 1 gallon tap water; make fresh daily).
4. Add 2% formaldehyde solution to reservoir; circulate solution through machine for 5 minutes.	See machine Operator's Manual for specific steps of formaldehyde procedure.
5. Follow instructions in section 4.3 of this primer for formaldehyde disinfection of infusate system.	To make 2% formaldehyde solution, add 300 ml 37% formaldehyde to 6 liters of tap water.
6. Turn machine off. Place cover on reservoir. Leave solution in machine for at least 12 hours.	
PRIOR TO NEXT TREATMENT	
7. Drain formaldehyde solution from machine and infusate system.	
8. Rinse machine and infusate system at least twice with water; perform residual formaldehyde test.	Obtain specimen for residual test from last water exiting drain hose after final water rinse. There is a recommended national standard for residual formaldehyde of 5 ppm or less.[3] Use Fast Formalert™ or other test proven capable of detecting 5 ppm of residual formaldehyde.
9. Six liter jug (plus 10 liter RINSE jug with REDY 2000) should be disinfected prior to each treatment.	Use bleach (700 ppm free chlorine solution). See Comment 3 above. It is unnecessary to disinfect the drain jug since its contents do not come into contact with the dialysate pathway.

[3]AAMI Recommendations for use of Formaldehyde in Hemodialysis, March 1985.

™Registered Trademark, COBE Laboratories, Inc., Lakewood, CO.

4.3 DISINFECTION OF INFUSATE SYSTEM

The infusate cup and cap-and-line assembly may be disinfected with either 1200 ppm free chlorine bleach solution, 34:1 Actril* solution or 2% formaldehyde solution.

REDY 2000

Bleach and Actril:

A. Rinse infusate cup with tap water.
B. Prior to turning power on for disinfection cycle, fill infusate cup with disinfectant solution from reservoir. Reattach infusate cup to system.
C. Turn power ON. AUTO CLEAN mode may be used for bleach only. Sequence system to MANUAL CLEAN mode if using Actril. Allow disinfectant to circulate through machine and infusate system for period specified for bleach or Actril in Section 4.2.
D. While machine is draining before first water rinse, remove infusate cup from machine. Flush cup thoroughly with water at sink then fill cup with water and reattach it to the machine.
E. After rinse cycles are completed, empty water from infusate cup.
F. Testing the infusate system for residual disinfectant is unnecessary if steps D and E are performed as directed.

Formaldehyde:

A. Prior to turning power on for disinfection cycle, fill infusate cup with formaldehyde solution from reservoir. Reattach infusate cup to machine.
B. With system in MANUAL CLEAN mode, turn power on and allow formaldehyde to circulate through machine and infusate system for at least 5 minutes.
C. Turn power OFF. Allow disinfectant to remain in system for at least 12 hours.
D. (Pre-dialysis) While machine is draining prior to first water rinse, remove infusate cup from machine. Flush cup thoroughly with water at sink then fill cup with water and reattach to machine.
E. Use two 5 minute rinse cycles. After rinse cycles are completed, empty water from infusate cup.
F. Testing the infusate system for residual formaldehyde is unnecessary if steps D and E are performed as directed.

OTHER REDY SYSTEMS

Bleach and Alkaline Glutaraldehyde:

A. Rinse infusate cup and cap-and-line assembly with tap water.
B. Place infusate cup under surface of disinfectant solution in reservoir. Ensure cup is completely full of disinfectant. Leave cup in reservoir throughout period disinfectant is circulated through machine.
C. Meanwhile, fill 20-30 ml syringe with disinfectant solution from the reservoir. Attach syringe to cap-and-line assembly and flush line with disinfectant. To avoid splashing disinfectant, keep open end of infusate line under surface of fluid in reservoir. Leaving syringe attached to line (to prevent disinfectant leaking out of line), drop cap-and-line assembly into reservoir.
D. When machine is drained prior to first water rinse, remove infusate cup and cap-and-line assembly from reservoir; set aside.
E. While first water rinse is circulating in machine, thoroughly flush infusate cup and cap-and-line assembly with running water at sink. Ensure that inside of infusate line is flushed with running water for at least 30 seconds.
F. Testing the infusate system for residual disinfectant is unnecessary if step E is performed as directed.

Formaldehyde:

A. After formaldehyde solution has been circulated through machine for 5 minutes and pumps have been turned off, place infusate cup into formaldehyde solution within reservoir. Ensure infusate cup is completely full of disinfectant.
B. Use 20-30 ml syringe to flush infusate line with formaldehyde. To avoid splashing formaldehyde, keep open end of infusate line under the surface of the fluid in the reservoir while flushing. Leaving syringe attached to line (to prevent disinfectant leaking out of line), drop cap-and-line assembly into reservoir.
C. Allow infusate cup and cap-and-line assembly to remain in reservoir until next machine use.
D. After formaldehyde has been drained from machine, remove infusate cup and cap-and-line assembly from reservoir.
E. Thoroughly rinse both with running water from sink tap. Ensure that inside of infusate line is flushed with running water for at least 30 seconds.
F. Testing the infusate system for residual formaldehyde is unnecessary if step E is performed as directed.

*Registered Trademark, Renal Systems, a Division of Minntech Corporation, Minneapolis, MN.

4.4 SPECIAL DISINFECTION PROCEDURES

4.4.A. Contaminated Equipment

When to use these procedures:
– Post dialysis, if a blood-to-dialysate leak has occurred with a patient known or suspected to have AIDS, any type of Hepatitis or other blood-borne infection of clinical concern.

Bleach Procedure

The 1200 ppm free chlorine solution is adequate for this procedure. Follow Routine Bleach Procedure **except**:

1. Bleach machine immediately post dialysis.
2. Circulate bleach through machine for **at least** 10 minutes (30 minutes at most), then drain. Use Manual Clean Mode on REDY 2000.
3. Rinse system at least twice with water, then drain.
4. Steps 5 and 6 of Routine Bleach Procedure must be repeated prior to next dialysis, unless another dialysis treatment is to follow immediately.

Formaldehyde Procedure

Follow Routine Formaldehyde Procedure **except**:

1. Use a 4% formaldehyde solution. To make 4% solution, add 600 ml 37% formaldehyde to 6 liters of water.
2. Allow 4% formaldehyde solution to remain in machine for a minimum of 12 hours.

4.4.B. Machine Storage – One Month or Less

Bleach or Peracetic Acid Method:
1. Post Dialysis – perform entire Routine Bleach or Peracetic Acid Procedure (steps 1-7).
2. Store machine drained. Make sure all machine covers are in place.
3. Perform entire Routine Bleach or Peracetic Acid Procedure immediately prior to next dialysis. Wipe down exterior of machine, cart, jugs, etc., with a hospital approved disinfectant.

Formaldehyde Method:
1. Post Dialysis – perform steps 1-5 of Routine Formaldehyde Procedure.
2. Store machine filled with 2% formaldehyde solution. Make sure all machine covers are in place.
3. Perform steps 6-8 of Routine Formaldehyde Procedure immediately prior to next dialysis. Wipe down exterior of machine, cart, jugs, etc., with a hospital-approved disinfectant.

4.4.C. Machine Storage – Prolonged Storage

Machines which are not expected to be used for a prolonged or indefinite period of time should be disinfected by one of the procedures recommended in Section 4.2, **then drained** and stored with all machine covers in place.

After prolonged storage, it is recommended that the machine be checked for proper function by a qualified dialysis or biomedical technician. Special attention should be paid to the conductivity probe, which often develops a film during dry storage which interferes with function.

Prior to use the entire machine, including jugs and infusate assembly, should be disinfected.

APPENDIX

5.1 DIALYSATE SAMPLING

5.1.A. Conductivity/Electrolyte Levels

Dialysate samples obtained near the perimeter of the reservoir are not representative of fully regenerated dialysate. This is because (1) the infusate chemicals and the cartridge effluent enter the reservoir at separate locations and, (2) these fluids enter down the side of the reservoir, from which they are gradually drawn into the mixing vortex in the center of the bath.

For these reasons, dialysate samples should be obtained from the center of the reservoir, where the fluids have been adequately mixed by the Cartridge Effluent Jet.

NOTE: The ideal method for obtaining dialysate samples is to draw them from a dialysate sampling port installed in the "To Dialyzer" hose. Sampling ports are available at modest cost from a variety of dialysis equipment manufacturers, including COBE Renal Care.

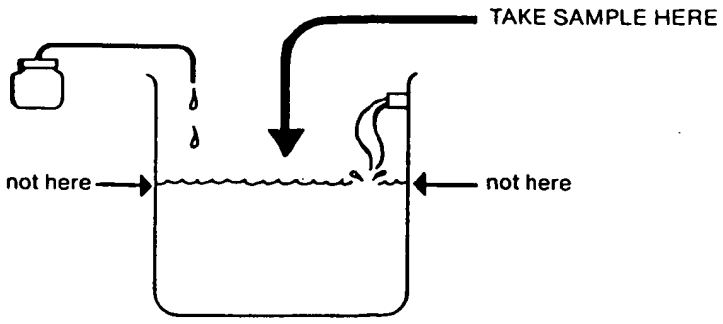


Figure A.1: Dialysate Sampling

5.1.B. DIALYSATE TEMPERATURE VERIFICATION

The dialysate in the reservoir tends to form layers of varying temperatures; however the dialysate does present a constant temperature to the dialyzer since it is drawn from a constant site in the reservoir. To confirm the dialysate temperature, stir the dialysate in the reservoir with a clean non-metallic implement, then measure the temperature and compare it to the temperature display on the front of the REDY.

NOTE: We recommend keeping the plexiglass cover in place over the reservoir to minimize dialysate heat loss and prevent unnecessary energy consumption by the heater. The cover also prevents stray objects from entering the dialysate and possibly jamming the pumps or valves of the internal dialysate pathway.

5.2 CALCULATIONS AND FORMULAS

5.2.A. Sodium

During dialysis with the REDY Sorbent system, besides a shift of sodium between the REDY system and patient, there is a constant addition of sodium to the system. This complicates the estimation of the patient's post-dialysis sodium level. However, if all the sources of sodium are summated and the volume relationships between the patient and REDY system are taken into consideration, then a good estimate of post-dialysis serum sodium can be made.

1. Sources of Sodium
   The major source of sodium is the patient. Sodium is present primarily in the extracellular volume. However, because water shifts between the extracellular and intracellular compartments in response to shifts in sodium, the sodium space is equivalent to the total body fluid. In these calculations we will assume that the sodium space is equal to 0.6 times the serum sodium (mEq/L).

   Another source of sodium is the dialysate. The initial dialysate volume is usually 6 liters. Therefore, the total sodium in the dialysate equals 6 (L) times the initial dialysate sodium concentration (mEq/L).

   The infusate system contributes sodium in that calcium, magnesium and potassium are exchanged for sodium in the zirconium phosphate layer. The amount of sodium contributed by the infusate is equal to the total concentration of Ca, Mg and K (mEq/L) added to the dialysate times the dialysate flow in milliliters/minute times the number of minutes of dialysis multiplied by .001 (to convert milliliters to liters).

   In the REDY system the urea removed from the patient appears as sodium bicarbonate, carbon dioxide and water in the dialysate.

   The amount of sodium is approximately 15% of the urea-nitrogen removed from the patient. The urea-nitrogen removed from the patient is equal to the expected drop in SUN times the total body fluid (0.6 times the body weight in kg) multiplied by 0.01 (a factor which both converts milligrams to grams and milliliters to liters). This amount of urea-nitrogen in grams divided by 0.014* gives the millimoles of urea-nitrogen removed. Fifteen percent of this is sodium in mEq.

   Some sodium is contributed to the dialysate from the sorbents and the saline prime. This amount, approximately 100 mEq, can be eliminated from the calculations since it is small compared to the other sources of sodium.

2. Volume Relationships
   A 70 kg patient has a total body fluid volume of about 42 L while the REDY system has a volume of only 6 L. Thus, during dialysis, the dialysate tends to equilibrate with the patient. However, sodium equilibration never takes place since sodium is constantly being added to the dialysate from the infusate and patient's urea. In general, the patient's sodium level lags behind that of the dialysate by approximately one hour. Therefore, for a 4 hour dialysis we will assume that ¾ of the sodium added by the infusate and patient's urea has been distributed between the patient and dialysate. For any dialysis time (t) we will assume that [(t - 1)/t] has been distributed. This is mathematically equal to 1 hour less than the dialysis time.

3. Estimation of Post-Dialysis Serum Sodium
   A. Assemble necessary information (data for a "standard" adult patient have been inserted here for purposes of illustration).

      Patient:
      Weight: 70 kg
      Serum Na: 138 mEq/L
      Pre BUN: 80 mg/dl – expected post BUN: 45 mg/dl
      Dialysis Time: 4 hours
      Fluid Volume: 0.6 x Total Body Weight in kg

      Dialysate:
      Sodium: 105 mEq/L
      Volume: 6 L
      Flow: 200 ml/min
      Infusate: 3 Ca, 1 Mg, 1 K mEq/L (Total: 5 mEq/L)

*The molecular weight of nitrogen, divided by 1000 to convert grams to millimoles.

5.2 CALCULATIONS AND FORMULAS (continued)

B. Calculate Sources of Sodium

Patient: 70 kg x 0.6 = 42 L body fluid	
42 L x 138 mEq/L =	5,796 mEq
Dialysate: 6 L x 105 mEq/L =	630 mEq
Infusate for ¾ of 4 hour dialysis – see Table A.1	180 mEq
Urea for ¾ of Total Sodium – see Table A.2	121 mEq
TOTAL SODIUM	6,727 mEq

C. Derive Estimated Post-Dialysis Patient Sodium[1]

$$\frac{\text{Total Sodium}}{\text{Total System Volume (Initial Patient + Dialysate Volume)}} = \frac{6727 \text{ mEq}}{48 \text{ L}} = 140 \text{ mEq/L}$$

140 mEq/L = Estimated Post-Dialysis Patient Sodium

TABLE A.1 Sodium from Infusate

Four Hour Dialysis

INFUSATE TOTAL (mEq/L)	¾ OF TOTAL SODIUM[2] DIALYSATE FLOW (mL/min) 200	250
3	108	135
4	144	180
5	180	225
6	216	270
7	252	315
8	288	360
9	324	405

TABLE A.2 Sodium from Patient's Urea

Four Hour Dialysis

UREA-NITROGEN ADSORBED BY CARTRIDGE[3] (gm)	¾ OF TOTAL SODIUM[2]
10	80
11	88
12	96
13	104
14	112
15	121
16	129
17	137
18	145
19	153
20	161
21	169
22	177
23	185
24	193
25	201
26	209
27	217
28	225
29	233
30	241

[1]These calculations have not been verified clinically

[2]Distributed between patient and dialysate during 4 hours of dialysis.

[3]Equals: (Pre SUN - Post SUN)(Body Fluid Volume)(0.01)

5.2.B. Bicarbonate

Approximately 15% of the urea passing through the Sorbent Cartridge is converted to sodium bicarbonate.
Example: 17 grams of urea-nitrogen is converted to 182 mEq of sodium bicarbonate

$$\frac{17 \text{ grams urea-nitrogen}}{14 \text{ grams/mole}} \times 0.15 \times 1000 = 182 \text{ mEq of sodium bicarbonate}$$

Where:
17 grams urea-nitrogen is the calculated amount of urea-nitrogen adsorbed by the Cartridge (see Appendix 5.2.D.);
14 grams/mole is the formula weight of nitrogen;
0.15 is the average percent conversion of urea to sodium bicarbonate by the Cartridge; and
1000 is the conversion of Eq to mEq.

5.2.C. Acetate

Calcium, magnesium, and potassium acetates are converted to sodium acetate when passed through the Sorbent Cartridge.
Example: An infusate providing 3.5 mEq/L calcium, 1 mEq/L magnesium, and 2 mEq/L potassium is converted to 312 mEq/L sodium acetate when passed through a Sorbent Cartridge during 4 hours of dialysis at a dialysate flow of 200 ml/min.
6.5 mEq/L (Ca/Mg/K) x 200 ml/min x 0.001 x 60 min/hr x 4 hr = 312 mEq

Where:
6.5 mEq/L is the total mEq of acetate from calcium, magnesium, and potassium acetates;
200 ml/min is the dialysate flow rate;
0.001 is the conversion from milliliters to liters; and
60 min/hr is the conversion from minutes to hours.

5.2.D. Cartridge Capacity

The capacity of the Sorbent Cartridge is limited by the amount of ammonia which can be adsorbed by the zirconium phosphate. This, in turn, limits the capacity of the Cartridge for urea. The SORB Cartridge has a urea-nitrogen capacity of approximately 20 ± 2 grams while the HiSORB has a urea-nitrogen capacity of approximately 30 ± 3 grams. Which Cartridge to use can be determined by calculating the estimated urea-nitrogen to be adsorbed by the Cartridge.

Example: A patient has a body weight of 70 kg and a serum urea-nitrogen of 80 mg/dl. Considering factors such as dialyzer clearance, dialysis duration, blood and dialysate flow rates, it is estimated that the SUN will be 45 mg/dl at the end of dialysis. The formula for the calculation to determine which Cartridge to be used is:

Expected drop in SUN(g/kg) x Body Fluid Volume(kg)

1. Expected drop in SUN.
   To convert mg/dl (or mg%) to g/kg, move the decimal point 2 places to the left. Thus, 80 mg/dl - 45 mg/dl = 35 mg/dl or .35 g/kg
2. Body Fluid Volume = Body Weight in kg x % Body Water
   Assuming this patient's body fluid volume comprises 60% of body weight,
   70 kg x .6 = 42 kg
3. Multiply the two results. .35 g/kg x 42 kg = 14.7 g

Therefore, a SORB Cartridge will be adequate.

5.3 RADIATION AND THE CARTRIDGE

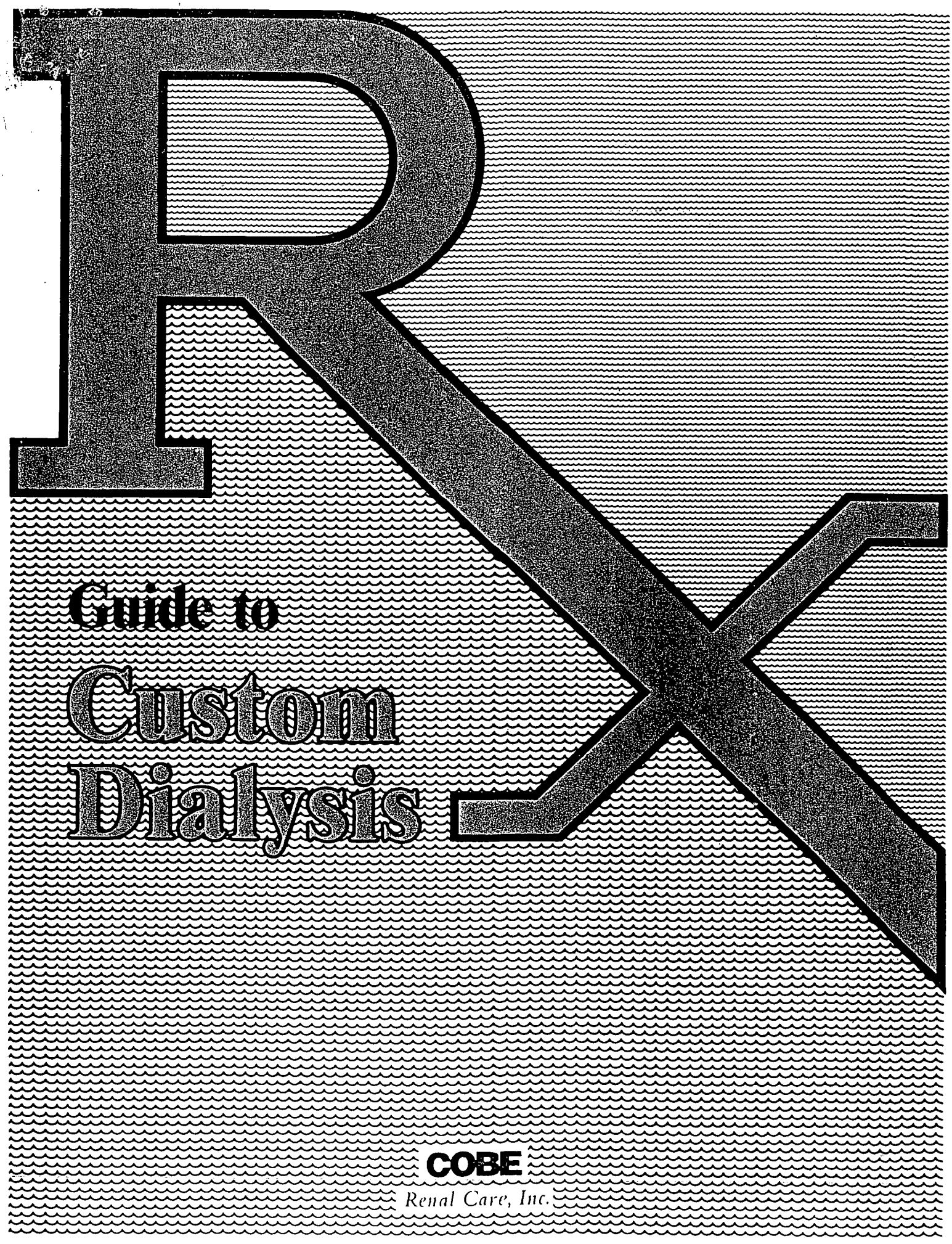
Occasionally a patient will arrive for dialysis shortly after having undergone a diagnostic procedure which involved the IV administration of a radioactive isotope. Most such isotopes will cross the dialyzer membrane and be carried by the dialysate into the sorbent cartridge, where they are bound. As a result, the cartridge becomes radioactive.

This raises two questions: Is the radioactive cartridge a danger to the staff? Does the radioactivity damage cartridge function? The answer to both is no.

A dose of radioactive isotope which is not dangerous to the patient is also not dangerous to the staff, whether the isotope is in the patient or the cartridge. However, if staff is very concerned, the cartridge can be covered with lead foil which is available from the hospital's Nuclear Medicine Department (the same people who administered the isotope to the patient). The Nuclear Medicine Department can also advise whether the radioactive cartridge should be placed in a shielded area for a specified period of time before being discarded with the trash.

Interestingly, zirconium sorbents were originally developed in the 1950's specifically for the atomic energy field because conditions of high radiation do not affect their function. The carbon layer is also unaffected. Very high doses of radiation (3 megarads or more) will decrease the activity of the urease layer but this is not a problem with cartridges exposed to diagnostic quantities of radioactive materials, as total doses are in the range of 15-200 microcuries (a fraction of a megarad).

The U.S. Atomic Energy Commission recommends radioactive wastes be absorbed and discarded in solid form whenever possible. Thus sorbent cartridges are a perfect medium for meeting the AEC recommendation, whereas, in the patient circumstances above, single pass machines release radioactive wastes into environmental water.


Rx
Guide to
Custom
Dialysis
COBE
Renal Care, Inc.

This Guide has been prepared for use by clinical personnel who are familiar and experienced with the equipment and principles of Sorbent Dialysis.

THIS IS NOT AN OPERATOR'S MANUAL FOR SORBENT DIALYSIS SYSTEMS. NOR IS THE MATERIAL HEREIN INTENDED AS A PRESCRIPTION FOR ANY PATIENT.

Only a physician can determine the dialysis prescription. If questions arise regarding these contents, please contact COBE Renal Care Customer Service Department at 1-800-525-2623.

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Product Number 306100-005 Printed in U.S.A. Revision E, 9-93

1. PRINCIPLES OF CUSTOM SORBENT DIALYSIS

2. CUSTOM DIALYSATES

3. ULTRAFILTRATION PROCEDURES

4. DIALYSATE PURIFICATION

5. DRUG OVERDOSE

APPENDIX

1.1. INTRODUCTION AND THE REDY SORBENT SYSTEM

INTRODUCTION

The acute renal failure patient with post-operative and/or multiple organ system failure and the unstable hospitalized chronic renal failure patient often present metabolic and hemodynamic abnormalities differing significantly from stable maintenance dialysis out-patients. Hemodialysis of such patients can be fraught with multiple problems. They may be on a ventilator, be hypotensive, hyponatremic, and hypokalemic. Mixed acid/base disorders and glucose intolerance are common. Such patients are often receiving total parenteral nutrition and multiple intravenous solutions resulting in fluid overload. They may be catabolic and/or have gastrointestinal bleeding. Serum urea nitrogen may be elevated, especially if adequate amounts of protein (1-1.5 gm/kg) are being administered. These patients, as well as the out-patient on maintenance hemodialysis with special problems, can best be treated by "custom dialysis" using individualized dialysates. Such dialysates are easily prepared for use with the REDY Sorbent System because of its small dialysate volume (6 L).

The REDY Sorbent System is significantly different from other dialysis systems. Therefore, its unique properties should be understood in order to optimally apply the system to patients requiring custom dialysis.

THE REDY SORBENT SYSTEM

The REDY Sorbent System is a regenerative dialysate delivery system using the unique five layer sorbent cartridge. Spent dialysate from the dialyzer flows through the sorbent cartridge which removes the waste metabolites. The regenerated dialysate leaving the cartridge consists essentially of sodium chloride, sodium bicarbonate, sodium acetate, carbon dioxide, and water. An infusate system adds calcium, magnesium, and potassium (as acetate or chloride salts) resulting in a fully regenerated dialysate for recirculation to the dialyzer. A detailed description of the cartridge is given in Appendix I.

The dialysate composition during dialysis does not remain constant. The cartridge and the patient add or subtract various solutes during dialysis, while the infusate system is maintaining dialysate calcium, magnesium, and potassium levels. Since the dialysate volume is small compared to the patient's total body fluid, the solute levels in the dialysate tend to quickly equilibrate to the patient's serum concentration unless additional quantities of the particular solute are added to or removed from the dialysate during dialysis.

A. Sodium

The initial dialysate sodium concentration depends upon the dialysate used. With sodium bicarbonate dialysates, the sodium level falls after the cartridge is inserted and for the first 30 minutes after the patient is placed on dialysis, due to the adsorption of sodium by the cartridge, and the formation of carbon dioxide. Subsequently, the sodium level increases as sodium bicarbonate becomes available from the hydrolysis of urea, and the exchange of sodium for ammonia in the zirconium phosphate layer. In addition, calcium, magnesium, and potassium from the patient and infusate are exchanged for sodium. The dialysate sodium can also be increased or decreased by the addition of concentrated sodium chloride or water, respectively. Failure to add concentrated sodium chloride or additional water can result in inadequate correction of the patient's hyponatremia or hypernatremia (Section 1.4B).

B. pH and Bicarbonate

The initial dialysate pH and bicarbonate level depend upon the dialysate used. Bicarbonate dialysates are neutralized by the addition of acid present in the kits. After the cartridge is inserted, and for the first 30 minutes after the patient is placed on dialysis, some of the dialysate bicarbonate is converted to carbon dioxide by the sorbent cartridge resulting in a fall in the pH and bicarbonate level. The dialysate pH and bicarbonate levels subsequently increase as bicarbonate becomes available from urea hydrolysis.

C. Calcium, Magnesium and Potassium

The initial sodium bicarbonate dialysates do not contain calcium or magnesium since precipitation would result. After addition of the acid from the bicarb kit, or fifteen minutes after inserting the cartridge, sufficient carbon dioxide has been formed, and the pH is low enough to permit the addition of calcium and magnesium. The initial chloride dialysates also do not contain calcium, magnesium or potassium. However, addition of 11 ml of infusate to each dialysate will bring the dialysate concentration of calcium, magnesium, and potassium to the desired level. The infusate system will then maintain the desired concentration of these cations.

D. Chloride

The chloride level in the initial dialysate varies with the dialysate used. As dialysis proceeds, the chloride concentration approaches the patient's serum concentration unless the infusate contains the chloride salts of calcium, magnesium, or potassium instead of acetates. In the latter case the chloride level slowly increases during dialysis.

E. Phosphate

No phosphate is present in the dialysate. Phosphate donated by the patient to the dialysate is removed by the sorbent cartridge in exchange for bicarbonate (or acetate) present in the hydrated zirconium oxide layer of the sorbent cartridge.

F. Acetate

With bicarbonate dialysate, no acetate is present in the initial dialysate. After the cartridge is inserted, some bicarbonate is exchanged for acetate from the cartridge. The acetate will then return to a low level as it is transferred to the patient and metabolized to bicarbonate. With an acetate infusate (calcium 3.5 mEq/L, magnesium 1.0 mEq/L, and potassium 2.0 mEq/L), 180 mEq from the cartridge and 312 mEq of acetate from the infusate, giving a total of 492 mEq, are added to the dialysate during a typical four hour treatment. This compares to 480 mEq of acetate with single pass bicarbonate dialysis, since 4 mEq/L of acetate is present in the bicarbonate solution as an acidifying agent.

G. Glucose (Dextrose)

A relatively small percentage of the glucose in the dialysate is adsorbed by the cartridge. The amount adsorbed varies with the dialysate glucose concentration. If the dialysate glucose level falls during dialysis, the cartridge will donate glucose to the dialysate. As dialysis proceeds, glucose is adsorbed and metabolized by the patient or donated by the patient until the dialysate glucose level approaches the patient's serum level.

1.2. OBJECTIVES OF CUSTOM DIALYSIS

The objectives of custom hemodialysis are diverse. They include the removal of metabolic waste products such as urea, creatinine, and other known and unknown toxic metabolic compounds; the normalization of pH and serum sodium and potassium levels; and the removal of excess fluid.

A. Remove Waste Products

The accumulation of nitrogenous waste products in the patient's serum depends upon the patient's protein intake, body weight, muscle mass, residual renal function, state of anabolism or catabolism, and the duration of time since the last dialysis. In addition, the increase in serum urea levels during the interdialytic period depends upon the amount of protein breakdown. In a stable patient, this amount is almost entirely due to dietary protein intake; in an acutely ill, hospitalized patient, urea may also be generated from the absorption of blood from the gastrointestinal tract and/or muscle protein breakdown. The rate at which waste products are removed depends upon the initial level of the substance, the duration of dialysis, the dialyzer clearance, and the blood and dialysate flow rates.

B. Normalize pH

The blood pH is controlled by both the lungs, which vary the level of dissolved carbon dioxide (pCO_2), and the kidneys, which alter the serum bicarbonate level. In healthy persons with normal respiratory function, the pCO_2 ranges from 36 to 44 mmHg.*

In acutely ill patients, several factors may directly lower the pCO_2; patients tend to hyperventilate (lower the pCO_2) with sepsis, cirrhosis, hypoxemia, congestive heart failure, pneumonia, and other pulmonary diseases. Also, patients on a respirator generally have a low pCO_2.

In a patient with impaired renal function, several factors may affect the bicarbonate level. Approximately 1 mEq of acid is formed for every gram of protein metabolized. This acid (H^+)

*It should be noted that the total CO_2 reported with the usual serum "electrolytes" is 95% bicarbonate and 5% dissolved CO_2 in patients with normal acid/base status. The pCO_2 reported with arterial blood gases is the partial pressure of dissolved CO_2 in the blood.

combines with bicarbonate in the serum, forming CO_2 and water, thereby reducing the bicarbonate level*. If protein metabolism is increased either by an increase in protein intake or by breakdown of a patient's muscle or blood protein, a greater quantity of acid will be produced and the fall in bicarbonate level enhanced. If the patient is in shock or has poor tissue perfusion for other reasons, he may be continuously generating lactic acid. Under these circumstances a fixed dialysate bicarbonate may be inadequate, and additional bicarbonate should be added to the dialysate or given intravenously.

An increase in serum bicarbonate will result from the parenteral administration of sodium bicarbonate or bicarbonate precursors such as acetate and lactate, especially in the renal failure patient who cannot eliminate the resultant bicarbonate. Nasogastric suction also removes hydrochloric acid, causing a relative increase in serum bicarbonate.

In addition to the primary factors affecting acid/base status discussed above, a varying degree of appropriate respiratory compensation occurs in response to changes in the bicarbonate level. For example, a patient with a low bicarbonate level due to metabolic acidosis normally would partially compensate by hyperventilating, thereby tending to raise the pH towards normal. Alternatively, a patient with an elevated bicarbonate level (metabolic alkalosis) will hypoventilate, increasing his pCO_2 level, thereby tending to lower the pH towards normal. If a patient is hyperventilating more than expected, he is said to have a concomitant primary respiratory alkalosis; if the pCO_2 is not as low as anticipated, he is said to have a concomitant respiratory acidosis; in these two instances, the patient has a mixed acid/base disturbance.

Figure 1: Acid-Base Abnormalities

			Mixed	
	Metabolic Acidosis	**Metabolic Alkalosis**	**Metabolic Acidosis Respiratory Alkalosis**	**Metabolic Alkalosis Respiratory Acidosis**
Serum Bicarb:	Below Normal	Above Normal	Below Normal	Above Normal
Blood pH:	Low	High	Low-Normal	Normal-High
pCO_2:	Low*	High*	Low	High
Respiratory Rate:	Hyper-ventilation	Hypo-ventilation	Hyper-ventilation	Hypo-ventilation

*Partially Compensated

Dialysis can only alter the bicarbonate level. If hyperventilation or hypoventilation is due solely to compensation for the metabolic disorder, the patient's respiratory response to change in bicarbonate level will be appropriate. However, if the patient, in addition to metabolic acidosis, has an independent drive to hyperventilate (respiratory alkalosis), an increase in the serum bicarbonate level with dialysis may not cause the pCO_2 to rise appropriately and the patient may become severely alkalemic.

A major objective of dialysis is to bring the pH towards normal, even if the bicarbonate level is not normalized. Therefore, it is imperative that the nature of the acid/base disorder be properly ascertained before attempting to alter the serum bicarbonate level with dialysis.

C. Adjust Sodium

With acutely ill patients, the serum sodium concentration often deviates from normal. An elevated serum sodium concentration (hypernatremia) is less common than a low serum sodium level (hyponatremia). Hypernatremia in a patient with renal failure often results from the administration of hypertonic sodium bicarbonate to treat severe metabolic acidosis, or during resuscitation following a cardiac arrest. Hyponatremia reflects a low serum sodium to water ratio, and, as is also the case with hypernatremia, can be present in a patient who is dehydrated, euvolemic, or fluid overloaded. A common cause for hyponatremia is the ingestion or administration of water while restricting sodium intake, thereby diluting the sodium concentration in the serum.

D. Normalize Potassium

Hyperkalemia is more frequent than hypokalemia in the stable, end stage renal disease patient because of the inability of the diseased kidney to excrete potassium. In contrast, normokalemia (potassium of 3.5 to 5.0 mEq/L) or hypokalemia (potassium less than 3.5 mEq/L) is quite commonly encountered in the hospitalized renal failure patient. The serum potassium may

be low if the patient is not eating and there is no breakdown in muscle protein (which would tend to release potassium). The potassium level should not be permitted to decrease to low levels during dialysis, especially if the patient is prone to arrhythmias or receiving digoxin, because digitalis toxicity may result.

Changes in pH influence the serum potassium concentration (Appendix III). As a patient becomes acidotic, hydrogen ions move into the cell, displacing potassium into the serum. Alternatively, as the pH increases (as, for example, with bicarbonate dialysis), hydrogen ions move out of the cells and potassium moves into the cells, causing a drop in serum potassium. The magnitude of the change is such that for each 0.1 change in pH the serum potassium will change in the opposite direction by 0.6 mEq/L. The infusion of dextrose in large amounts may also decrease the serum potassium concentration by driving a significant amount of potassium back into the cell. For these reasons, it is often necessary to individualize the concentration of potassium in the dialysate.

E. Balance Body Fluid Volume

With excess oral or parenteral fluid intake, anuric patients will become overhydrated between dialysis treatments. One of the objectives of hemodialysis is to remove this excess fluid. Fluid can be removed either during dialysis or prior to treatment by a procedure called "isolated" or "sequential ultrafiltration-hemodialysis". This method of fluid removal may be advantageous for the hemodynamically unstable patient. It should be noted that ultrafiltrate (whether "isolated" or during dialysis) is isotonic to the patient's plasma. For this reason, no change in serum sodium will occur due to ultrafiltration alone. Only a relatively small amount of the total waste products are removed by the ultrafiltration process since they are also present isotonically in the ultrafiltrate.

F. Stabilize Calcium

Patients with renal failure are often hypocalcemic. Hypocalcemia is caused by a combination of hyperphosphatemia, a decreased dietary calcium intake, and impaired intestinal absorption of calcium. Therefore, in order to increase the patient's calcium level, the dialysate commonly used for hemodialysis has a calcium concentration higher than the ionized ("free") calcium in the plasma of the average renal patient. It has been shown that a dialysate calcium concentration of 3.5 mEq/L is probably best for the average dialysis patient. This is equivalent to 7 mg/dl.*

1.3. CARDIOVASCULAR INSTABILITY: OVERALL APPROACH

A. Bicarbonate

Bicarbonate is used instead of acetate in the custom dialysates since dialysates which contain bicarbonate as the base have been demonstrated to cause less hypotension. Five basic dialysates have been formulated, three with the initial dialysate varying from 20 to 100 mEq/L of bicarbonate, and two with initial dialysate containing 120 mEq/L sodium chloride but no bicarbonate. The dialysate which best normalizes the patient's arterial blood pH should be used.

B. Sodium

It is probably advantageous to provide sodium-poor solutions between dialyses to the hemodynamically unstable patient with a precarious cardiovascular system. Such sodium-poor solutions reduce the possibility of congestive heart failure in an oligoanuric patient with no renal or extrarenal sodium loss (such as diarrhea, vomiting, or gastrointestinal drainage). The serum sodium concentration will fall, thereby allowing the use of a high dialysate sodium concentration (150 to 165 mEq/L) to return the serum sodium concentration to normal. The use of such a high dialysate sodium concentration will reduce the incidence of disequilibrium and hypotension during dialysis.

C. Dextrose

The addition of dextrose to the dialysate will tend to decrease the incidence of disequilibrium and provide calories, in addition to supporting the patient's plasma osmolality. Hypoglycemia in the malnourished patient, whose glycogen stores are depleted, will be avoided. For routine

*The "free" ionized calcium is approximately equal to 50 to 60% of the total serum calcium. Thus, if the patient's calcium is 8 mg/dl, then the "free" calcium is 4 mg/dl (2.0 mEq/L) and a positive calcium balance will result with a dialysate containing 7 mg/dl (3.5 mEq/L).

dialysis, 48 grams of dextrose are added to the initial dialysate. A larger amount of dextrose, 96 to 120 grams, can be added to the dialysate for the patient with a high SUN level who may be prone to disequilibrium. However, one must be aware of the possibility that with these larger amounts of dextrose, hypoglycemia may occasionally result post-dialysis unless dextrose is continued intravenously or given orally.

If the patient is receiving parenteral nutrition via a peripheral vein (a method which provides insufficient carbohydrate calories), the additional 350 to 400 carbohydrate calories absorbed from the dialysate is of considerable benefit. For patients with a tendency towards hyperglycemia, an intravenous bolus of 5 to 25 units of insulin administered at the start of dialysis results in a more controlled serum glucose concentration post-dialysis.

D. Albumin

If the patient has a low serum albumin (under 3.5 g/dl), the intravenous administration of relatively large amounts of salt-poor 25% albumin often facilitates fluid removal with maintenance of blood pressure. Patients frequently require 25 to 75 grams (100 to 300 ml) or more of albumin during the dialysis procedure. The resulting increased serum albumin level may decrease the frequency of hemodynamic problems with subsequent dialyses.

1.4. DIALYSATE SELECTION

A. Acid/Base

1. General Considerations

The first consideration in selecting the most appropriate dialysate for a given patient is the blood pH. Measurement of the pH and blood gases provides the pCO_2 and bicarbonate levels, allowing the determination of the acid/base status and indicating whether there are underlying respiratory problems. If there is **no respiratory problem,** then the total CO_2, as measured with the electrolytes, can indicate whether metabolic acidosis or alkalosis is present.

The goal of hemodialysis is to normalize the pH. The pH depends upon the ratio of HCO_3 to pCO_2. Dialysis can change the bicarbonate concentration, while the patient's respiration changes the pCO_2. ***Normalizing the bicarbonate will not normalize the pH if the patient has an associated respiratory disorder.***

For an increase in serum bicarbonate greater than 10 mEq/L, the dialysate for severe acidosis should be selected (Table 1) or sodium bicarbonate should be given intravenously. If an increase in serum bicarbonate concentration of 4-9 mEq/L is desired, then the dialysate for moderate acidosis is selected. When an increase in serum bicarbonate of 2 to 4 mEq/L is desired, the dialysate for mild acidosis should be used. For no change in serum bicarbonate level, the dialysate for normal acid/base should be chosen. To decrease the serum bicarbonate concentration, the dialysate for alkalosis should be utilized.

Table 1: Dialysates to Adjust the Blood Bicarbonate

Patient's status	Desired Δ serum bicarbonate[a] (mEq/liter)	Dialysate solution: Sodium bicarbonate[b] (mmol/liter)	Dialysate solution: Sodium chloride (mmol/liter)	Dialysate solution: Dextrose (gm/liter)	Initial dialysis solution conductivity[c] (mMho)	Infusate anion
Severe acidosis[a]	> 10	100	40	8	11.4	Acetate
Moderate acidosis	4 – 9	60	80[d]	8	13.4	Acetate
Mild acidosis or normal acid-base	2 – 4	20	120	8	14.0	Acetate
Mild alkalosis	−4 – 0	0	120	8	12.7	Acetate
Severe alkalosis	< −4	0	120	8	12.7	Chloride

[a] Select the Δ bicarbonate value required to normalize the patient's pH.
[b] Based upon a 4-hour dialysis and bicarbonate generation in the cartridge consequent to adsorption of 16gm of urea.
[c] The conductivity values for these initial dialysis solutions fall outside of the shaded area shown in Fig. 3 due to their unusual chloride-bicarbonate ratios (see text). The conductivity values listed are valid only prior to addition of acidifier and 11 ml of infusate; they will no longer be applicable once the solution has circulated through the cartridge or after dialysis has begun, because then the chloride-bicarbonate ratio of these solutions will have changed.
Source: Modified from M. Roberts and M. J. Blumenkrantz. REDY Sorbent Hemodialysis System. In A. R. Nissenson (ed.). *Dialysis Therapy*. Philadelphia: Hanley & Belfus, 1986. With permission.
[d] For hypernatremic patients, omit the optional sodium chloride additive (7g packet, see p. 21.) thereby decreasing initial dialysate sodium level to 120 mEq/L and initial conductivity to 10.5 mMho.

REDY COMPUTE, a sorbent dialysis computer program, can be used to project the results of patient exposure to any of the custom dialysates.

In patients with complicated acid/base abnormalities, blood gases should be measured periodically during dialysis and particularly at 90 minutes prior to termination of dialysis so that necessary adjustments can be made. The patient should not have a markedly elevated serum bicarbonate prior to surgery since placing the patient on a ventilator may cause a low pCO_2, resulting in alkalemia.

2. Acidosis

Selection of which dialysate to use for an individual situation must also take into consideration the anticipated amount of urea to be removed and infusate acetate to be added to the dialysate since with the REDY Sorbent System the formation of bicarbonate is linked to these two substances. The anticipated amount of urea to be removed can be estimated from the expected drop in the patient's serum urea-nitrogen (Appendix 3). The expected drop in the patient's serum urea nitrogen depends upon the patient's total body fluid, dialyzer clearance, and dialysis time. Thus, large patients with a high Serum Urea Nitrogen (SUN) will contribute more urea to the sorbent cartridge, resulting in an increased formation of bicarbonate. Small patients with a low SUN will contribute less urea, giving little bicarbonate. Section 1.5 provides information on correction of acidemia in this and other circumstances that prevent adequate bicarbonate generation by the cartridge.

The Sorb 10 infusate mixture (3 mEq/L calcium acetate, 1 mEq/L magnesium acetate) provides a dialyzer exposure of 60 mEq acetate per hour if the dialysate flow rate is 250 ml/min (REDY 1000 and REDY 2000) or 48 mEq/hr for 200 ml/min dialysate flows (REDY URS, SORBSYSTEM SSD); by contrast, acetate exposure is 120 mEq/hr with most single pass bicarbonate dialysates. Addition of potassium and/or extra calcium or magnesium acetates to the infusate will slightly increase this value. Only part of the acetate to which the dialyzer is exposed trasfers into the patient. Too small to result in symptoms of acetate intolerance, this amount of acetate nevertheless contributes significantly to correction of acidemia. For this reason, the use of chloride infusates with bicarbonate dialysates is contrainicated.

3. Alkalosis

The anion in the dialysate for normal pH/mild alkalosis consists primarily of chloride, with a small amount of acetate provided by the infusate. The latter can vary between 8 and 15 mEq/L depending on the prescription for potassium, calcium and magnesium in the infusate and on the dialysate flow of the sorbent equipment. The purpose of this dialysate is to maintain the serum bicarbonate of an adult at or very slightly (1-3 mEq/L) below predialysis values.

The dialysate for severe alkalosis contains only inorganic anion (chloride), since it ultilizes chloride infusate. As a result, this dialysate presents a significant concentration gradient to the patient with respect to bicarbonate. This will cause a substantial decrement in blood bicarbonate levels. Severely alkalemic patients are rarely uremic, so very little organic anion enters the dialysate from the cartridge during the procedure. However, since the cartridge will not remove bicarbonate transferred into the dialysate by the patient, the dialysate eventually equilibrates with the patient. Blood gases drawn near the equilibration point approximately 2-3 hours into dialysis will indicate the degree of correction obtained; if it is not sufficient, the contents of the reservoir can be drained and replaced with fresh sodium chloride dialysate to restore the concentration gradient. Eleven milliliters of infusate should be added to this fresh dialysate to replete Ca, Mg and K levels.

B. Sodium

1. Normonatremic Patient

Once a suitable dialysate for normalizing acid-base balance has been selected from Table 1, the sodium level of that dialysate should be adjusted. If the patient is normonatremic predialysis, the dialysate sodium can be adjusted to 120 mEq/1 initially and allowed to increase during dialysis, as is normally done with chronic sorbent dialysis patients (Sorbent Dialysis Primer, COBE Renal Care, Chapter 2.3). Alternatively, the dialysate sodium can be maintained at a constant level. For patients with normal serum sodium, the initial dialysate sodium is adjusted, if necessary, to 140-150 mEq/L as recommended in Figure 2 by the addition of a small amount of Sodium Adjustment Solution (Chapter 2, Section 3) and subsequently maintained at a conductivity of 13.5-14.0 mMhos by removing a liter of dialysate and replacing it with a liter of water whenever necessary during dialysis.

2. Hyponatremic Patient

Mild hyponatremic can be corrected by adding 100 ml of Dialysate Sodium Adjustment Solution (Chapter 2.3) to the dialysate whenever necessary during dialysis in order to maintain the dialysate sodium at 150-155 mEq/L (conductivity 14.0-14.5 mmhos).

Unless additional sodium is added as described, hyponatremia may not be corrected since 6 L of dialysate contains an inadequate amount of sodium to cause a significant increase in the serum sodium concentration in an adult.

Moderate hyponatremia may also be corrected safely by using the 155-160 mEq/L dialysate sodium recommended in Figure 2. However, rapid correction of severe hyponatremia theoretically may provoke Osmotic Demyelinization Syndrome; for this reason, it is recommended dialysate sodium levels be maintained at no higher than 15 mEq/L above the predialysis plasma sodium. (Sterns RH, Silver SM. *Seminars in Dialysis,* 3:3-4, 1990.)

3. Hypernatremic Patient

Mild hypernatremia can be corrected by periodically replacing a liter of dialysate with a liter of water in order to maintain the dialysate conductivity at 12.5-13.0 mmhos during dialysis.

For more severely hypernatremic patients (serum sodium above 151 mEq/L), it is important that the sodium concentration be lowered slowly since a rapid fall in serum osmolality may cause excessive intracranial pressure. When serum sodium is between 151-160 mEq/L, the dialysate selected should be adjusted whenever necessary during dialysis substituting a liter of water for an equal amount of dialysate in order to maintain the conductivity between 12.5 and 13.0 mmhos. For the rare treatment that requires frequent dilution, 2.5 mL of infusate should be added to each liter of water to maintain dialysate Ca, Mg and K concentrations.

Caution should be exercised in attempting to correct the plasma sodium level in patients with very severe hypernatremia (serum sodium above 160 mEq/L) especially if serum urea nitrogen level is above 100 mg/dl since excessive intracranial pressure is likely to result. Volume overload, if present, should be reduced by isolated ultrafiltration and the plasma sodium concentration slowly reduced to about 160 mEq/L by intravenous infusion of 5% dextrose in water. Dialysis should be performed with a high dialysate sodium to prevent a drop in plasma sodium while reducing the urea level. The hypernatremia can be normalized, by maintaining dialysate conductivity between 12.5 and 13.0 during a subsequent dialysis once the predialysis SUN is below 100 mg/dl.

Figure 2: Normalization of Serum Sodium

NORMALIZATION OF SERUM SODIUM		
Patient Sodium (Pre-Dialysis) (mEq/L)	**Required 6 L Dialysate Sodium (mEq/L)**	**Maintain Conductivity* at: (mmhos)**
Severe Hypernatremia (Na over 151)	See Text	
Mild Hypernatremia (Na 145-150)	135-140	12.5-13.0
Normal Sodium (Na 135-144)	140-150	13.5-14.0
Mild Hyponatremia (Na 130-134)	150-155	14.0-14.5
Moderate Hyponatremia (Na 125-129)	155-160	14.5-15.0
Severe Hyponatremia (Na below 124)	See Text	

For method, see Section IV, B.
*Beginning 30 minutes after initiation of dialysis

4. Sodium Bicarbonate Dialysate Conductivity

Conductivity, a measurement of the ease with which an electric current can pass through an electrolyte solution, is primarily a measurement of the cation content of dialysate. Since sodium is by far the most prevalent cation in dialysate, conductivity can be a useful indicator of dialysate sodium concentration.

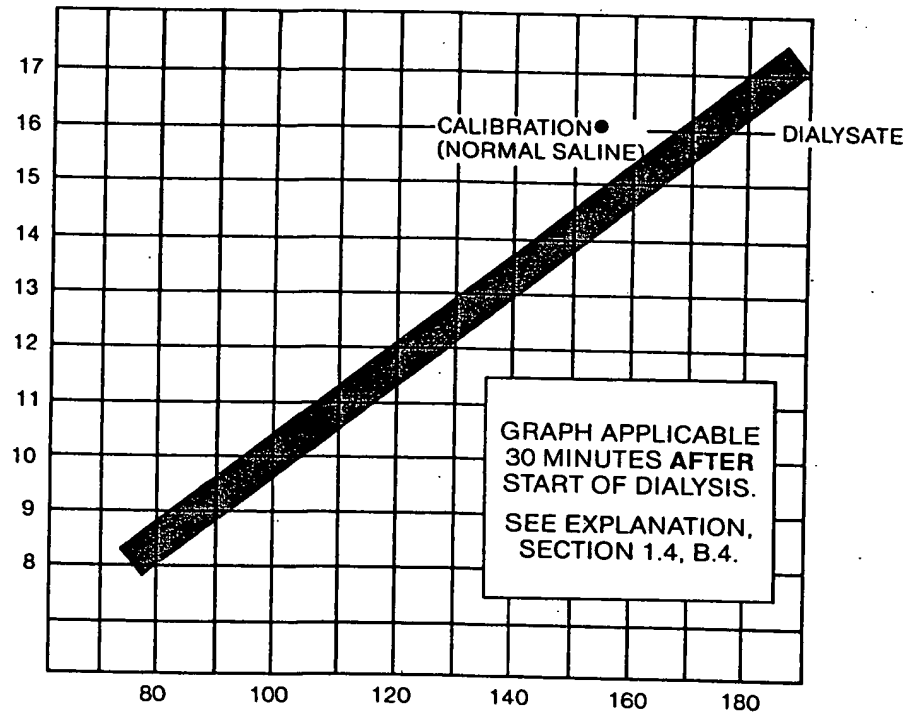
However, the relative concentrations of the anions in dialysate also affect conductivity. Inorganic anions, such as chloride, are better conductors of electricity than organic anions such as acetate and bicarbonate. As a result, two solutions with precisely the same sodium (and other cation) concentrations but different anions (chloride vs. bicarbonate, for instance) will have somewhat different conductivities.

The Sodium vs. Conductivity graph (Figure 3) presented in this section is based on a standard acetate sorbent dialysate which contains a mixture of sodium chloride, sodium acetate, and sodium bicarbonate. The custom bicarbonate baths recommended in Chapter 2 initially contain amounts of chloride and bicarbonate that vary from each other and from the solution on which the graph is based.

Thus, the sodium level in *initial dialysates,* once adjusted to the appropriate value in Figure 2 by adding the necessary amount of water or sodium chloride, *should be verified by flame photometry only.* About 30 minutes after dialysis is begun, the patient, cartridge, and infusate will have donated sufficient anions to render the dialysate composition equivalent to that used to make the graph. From that point — but not before — the graph is an accurate indicator of dialysate sodium concentration.

Dialysis machine conductivity readings should be verified with an independent conductivity meter at the beginning of each treatment. *If frequent bath adjustments with water or sodium adjustment solution are necessary to maintain a specific conductivity, machine conductivity should be verified hourly with an independent meter.*

Figure 3: Sodium Concentration vs. Conductivity



C. Fluid

Fluid removal with minimal hypotension during hemodialysis is facilitated by the use of bicarbonate dialysate with a high dextrose and sodium concentration plus intravenous albumin administration to support the intravascular volume. For circumstances where this combination is not possible or is ineffective, sequential ultrafiltration-hemodialysis is often successful (Chapter 3). Since very little urea is removed during isolated ultrafiltration, the total dialysis time must not be reduced. The amount of fluid removed can readily be determined by observing the increase in volume or weight of the dialysate reservoir of the Sorbent System.

D. Potassium

A severely hyperkalemic patient may require a dialysate with a potassium of 0 or 1 mEq/L. For such patients the serum potassium concentration should be measured midway through the dialysis and if the serum potassium has dropped below 5 mEq/L, the dialysate potassium should be increased to 2-3 mEq/L. The potassium level should not be permitted to fall too low during dialysis if the patient is prone to arrhythmias or receiving digoxin because digitalis toxicity may result. For digitalized patients or patients with hypokalemia, the dialysate potassium should be adjusted to 3-4 mEq/L. For the non-digitalized patient with a serum potassium of 4.5 to 6.0 mEq/L, a dialysate level of 2 mEq/L is recommended.

E. Calcium

To raise the serum calcium significantly in a markedly hypocalcemic patient, the dialysate calcium may be increased to levels as high as 4.5 mEq/L. For the treatment of the hypercalcemic patient, the dialysate calcium can be decreased to 0-2 mEq/L. This should be done with caution. A dialysate calcium concentration of 3.5 mEq/L is recommended for most patients.

With bicarbonate dialysates, the initial dialysate contains no calcium because the presence of calcium would result in a precipitate of calcium carbonate. After addition of the acid in the Bicarb Kit, or during the 15 minute cartridge titration period prior to starting dialysis, carbon dioxide is generated in sufficient quantities to prevent calcium precipitation. Eleven ml of infusate can then be safely added to the dialysate to bring the calcium level to the desired concentration. Thereafter, the infusate maintains the desired calcium concentration. Thus, the concentration of calcium in the dialysate depends solely upon the infusate.

The SORB 10™ Infusate Packet provides 3 mEq/L calcium and 1 mEq/L magnesium. The calcium concentration in the infusate can be adjusted by the addition of Ca-½ Infusate Additive. Each Packet, when added to the infusate, increases the dialysate calcium concentration by 0.5 mEq/L.

On rare occasions, it may be necessary to use a calcium-free dialysate to treat hypercalcemia. With sorbent systems it is easy to provide calcium-free dialysis.

The dialysate is prepared by using:

1. Low Calcium Water.
   If tap water calcium is above 2 mEq/L or is unknown, use RO or DI water.
2. Calcium-Free Infusate.
   Instructions for making calcium-free infusate are provided in Ch. 2.4. The resulting dialysate is also magnesium-free. **The prescription should specify whether magnesium is required,** as it can be added by the operator if necessary.

F. Dextrose (Glucose)

Dextrose is routinely added to dialysate in order to maintain plasma osmolality. This will not only reduce disequilibrium and assist in maintaining blood pressure, but also help avoid hypoglycemia in the diabetic or malnourished patient whose glycogen stores are depleted.

In single pass dialysis, dialysate dextrose levels of 150-200 mg/dl are generally used to maintain or, if necessary, replete patient blood glucose levels. During a 4-hour single pass dialysis with a 200 mg/dl dextrose dialysate, a normoglycemic adult patient will gain approximately 30 gm of dextrose.

Due to the much smaller volume of dialysate in sorbent systems, a higher concentration of glucose is necessary in order to achieve the same results. For routine dialysis, 48 grams of dextrose should be added to the dialysates, which will provide an initial dialysate dextrose concentration of 800 mg/dl. Once the dialysate has been exposed to the cartridge, this level will drop by approximately one third. The patient's large body fluid volume, compared to the small (6 liters) volume of dialysate, will prevent the blood sugar level from rising to that of the dialysate. Instead, the adult patient will gain approximately 30 gm dextrose during a 4-hour procedure, an amount equivalent to the dextrose transferred during single pass dialysis with a 200 mg/dl dextrose dialysate. Change in the insulin dosage of diabetics is normally unnecessary.

The amount of dextrose can be varied to meet the needs of the individual patient. The information in Table 2 is provided to indicate the effects on the average adult of various amounts of dextrose in 6 liters of dialysate.

Table 2: Dialysate Dextrose

Initial Dialysate		Amount Absorbed by Patient*	
Dextrose (gm)	Concentration (mg/dl)	Dextrose (gm)	K Cal
0	0	−12	− 45
6	100	− 4	− 15
12	200	+ 4	+ 15
24	400	+12	+ 45
48	800	+30	+112
96	1600	+58	+217

*These figures are approximate and will vary depending upon dialyzer clearance, dialysis time, patient serum glucose and volume of ultrafiltration.

G. Mannitol

The amount of mannitol which can be removed from the patient during dialysis is limited by the technique of dialysis, be it by single pass or by the sorbent system. In the course of a routine dialysis, approximately half of the patient's urea is removed. Since mannitol has a lower clearance than urea and is dialyzed for less time (since it is usually given during dialysis) less than 50% will be removed. The mannitol which remains is poorly metabolized, thus some practitioners advise that mannitol should not be used in patients who have no kidney function.

With the REDY Sorbent System, mannitol dialyzes until equilibrium is reached. Assuming that the dialysate volume (including ultrafiltrate) is 20% of the volume of distribution of mannitol in the patient, then this amount of mannitol will be removed when the dialysate is discarded at the end of dialysis. The additional amount of mannitol removed by the cartridge will be about one-half of the amount in the dialysate. Thus, about 30% of the mannitol given the patient will be removed by the sorbent system. This amount is not significantly different clinically than the less than 50% removed by single pass systems.

H. Citrate Anticoagulation

As stated in the SORB® and HiSORB™ cartridge insert (P/N 9079-601), ***citrate anticoagulation should not be used with sorbent cartridges.***

Citrate anticoagulant may affect the integrity of the cartridge, causing significant patient side effects. cartridge integrity is not affected using heparin as the anticoagulant.

COBE Renal Care does not recommend citrate anticoagulation during sorbent hemodialysis. For further information, contact the Customer Information Center at 1-800-456-7339.

1.5. SPECIAL CONSIDERATIONS

The dialysate selection process described in the previous section was developed for application to uremic adults undergoing a treatment of 4 to 5 hours in duration. If the patient is not uremic, is a child or adult who weighs less than 40 kg, will be dialyzed for 3 hours or less — or some combination of these factors — the following guidelines should be considered.

A. Short Treatment Time (2-3 hours)

1. Sodium

Short treatment time will result in less sodium becoming available from the cartridge for transfer to the patient, thus an initial dialysate sodium of 135 - 140 mEq/L should be used for normonatremics. The recommendations in Figure 2 (Normalization of Serum Sodium) are effective for patients who are not normonatremic.

2. Bicarbonate

When dialysis time is abbreviated, the patient may not transfer enough urea to generate adequate bicarbonate from the sorbent cartridge to provide correction of acidosis, particularly if the acidosis is severe. In addition, the patient is exposed to a smaller quantity of bicarbonate precursor from infusate chemicals. Therefore, it is recommended that the next higher bicarbonate dialysate formula be used. In severe acidosis, blood gases should be monitored so that dialysate or IV bicarbonate supplementation can be provided, if necessary.

3. Removal of Uremic Toxins

At dialysate flows of 500 ml/min or more, the concentration gradient between patient and dialysate changes very rapidly during the first 90-120 minutes of treatment and very little thereafter. This can be a problem for acutes, who are unstable by definition. The 250 ml/min dialysate flow rate of sorbent systems is advantageous in dialysis of severely uremic patients, as it affords extra protection against dialysis disequilibrium syndrome by decreasing the rate of change of pH, urea and sodium abnormalities. When treatment duration is 4 hours or more, net clearance is similar to that obtained in the same period with higher dialysate flows (assuming dialyzer type, blood flows, etc. are equivalent). However, when treatment time is less than 3 hours, the correction of uremia may be less than desired. This effect can be compensated by selecting a dialyzer with higher clearance values, by increasing blood flow rate, or both.

B. Non-uremic Patients

Occasionally it is necessary to dialyze a patient who is not uremic. Such patients represent a special subgroup in sorbent dialysis. When the patient cannot provide sufficient urea (at least ten grams, presented to the cartridge over a 3-4 hour period), the cartridge cannot produce enough CO_2 and bicarbonate to increase dialysate pH and bicarbonate levels. Thus acidosis will not be corrected and, in rare instances, may worsen. For this reason, patients who cannot present sufficient urea to the cartridge should receive supplemental bicarbonate during sorbent dialysis. This can be provided by periodic addition of sodium bicarbonate to the dialysate (five grams of $NaHCO_3$ will raise the bicarbonate concentration by 10 mEq/L) or to the patient, via administration of parenteral bicarbonate solutions into the venous blood line. Blood pH and bicarbonate levels, drawn periodically (but definitely 90 minutes prior to the end of dialysis), can be used as a guide for bicarbonate supplementation.

C. Pediatric and Small Adult Patients

As body fluid volume more closely approaches the volume of the dialysate in the sorbent system, the biochemical relationship between patient and dialysate more closely approximates that of single pass dialysis. This does not affect ultrafiltration, the removal of uremic toxins, or correction of potassium, calcium or magnesium imbalances but has some implications with respect to sodium and bicarbonate.

1. Sodium

If the patient is normonatremic, dialysate sodium should be maintained at 135-140 mEq/L throughout the dialysis by using the method described in Section 1.4B of this chapter. The recommendations in Figure 2 (Normalization of Serum Sodium) are effective for patients who are not normonatremic.

2. Bicarbonate

Small uremic patients may not transfer enough urea for the sorbent cartridge to generate adequate bicarbonate to correct their acidosis, particularly if the acidosis is severe. For this reason, it may be necessary to select a dialysate providing more bicarbonate than that indicated in Table 1 (Dialysates to Adjust the Blood Bicarbonate) for the patient's degree of acidemia. Alternatively, during the dialysis, bicarbonate can be added to the reservoir or parenterally via the venous bloodline. Each gram of $NaHCO_3$ added to the reservoir during dialysis will raise the dialysate bicarbonate concentration by 2 mEq/L. It is recommended that blood gases be monitored as a guide to supplementation.

D. Patients with Other Major Organ Damage

Providing hemodialysis for unstable acutes can pose a number of technical challenges, especially when the renal failure is associated with the functional impairment of other major organs. This section presents the methods of providing sorbent regenerative hemodialysis in patients with liver failure, ventilator-dependent pulmonary function impairment, and post-open heart surgery.

1. Liver Failure

Patients with combined liver and renal failure present a broader spectrum of metabolic waste to the dialyzer membrane. Consequently, bilirubin, ammonia, and other substances with molecular weights below 10,000 Daltons and normally cleared by the liver are presented to the sorbent cartridge, in addition to the uremic waste products in used dialysate. Most of these substances are adsorbed by the cartridge but two deserve special attention.

Bilirubin is adsorbed by the carbon layer of the cartridge but the amount of bilirubin that enters the dialysate of patients with significant hepatic failure exceeds the capacity of the carbon layer. Thus, bilirubin will accumulate in the dialysate until the level equilibrates with that of the patient. Consequently, the dialysate may become so yellow that a false blood-leak alarm may be elicited.

Also, the ammonia present in the blood of hepatic failure patients readily crosses the membrane and, combined with the ammonia produced by the urease-catalyzed conversion of urea, results in early saturation of the ammonia binding sites in the zirconium phosphate layer of the sorbent cartridge. Thus, in these cases, ammonia testing of the cartridge effluent should be performed every 15 minutes throughout the dialysis, after the first hour.

The above situations are dealt with by changing the cartridge whenever the ammonia test is positive and/or the dialysate is visibly yellow. While changing the cartridge is rarely necessary when dialyzing for uremia alone, it is common in the case of combined hepatic

and renal failure – and may be required as often as every hour during the early part of treatment of severe cases. Failure to do ammonia testing and change the cartridge when indicated can result in preventable patient morbidity (Canzanello, et al, 1983).

2. Ventilator-Dependent Patients

Exposure to bicarbonate-containing dialysate not only prevents the patient losing CO_2 to the dialysate, as initially occurs with acetate dialysis, but results in a rapid increase in the patient's total CO_2 as the bicarbonate entering the patient is utilized to neutralize the acidosis of uremia. Nevertheless, the production of CO_2 from bicarbonate is minor compared to that formed by basal metabolism and is readily expired by patients with reasonably normal pulmonary function.

However, there are two exceptions. The first is patients with compromised pulmonary reserve (i.e., severe COPD) or who are ventilator-dependent (i.e., respiratory rate and depth controlled by ventilator). In these cases, the patient cannot increase his respiratory rate to remove the extra CO_2 and may be at risk of developing hypercapnia, especially when high bicarbonate dialysates are used.* This risk is dependent on the bicarbonate and CO_2 level of the dialysate and not on the machine used to deliver the dialysate. Thus, intradialytic blood gasses should be closely monitored in ventilator-dependent patients so the ventilator rate can be increased as necessary to maintain CO_2 at desired levels.

The second exception is patients, ventilated or not, who have a mixed acid-base disorder – specifically, metabolic acidosis (due to the uremia) combined with respiratory alkalosis (due to a pulmonary disorder). This acid-base disorder is common in acute dialysis patients but is often not recognized. Rapid correction of the acidosis (i.e., by a high bicarbonate dialysate) will decompensate the alkalosis and there is a risk the patient will become hypercapnic due to hypoventilation. Such patients do better if the acidosis, which is usually very severe, is gradually corrected over several treatments.

In fact, patients with compromised pulmonary reserve may benefit from acetate dialysis, wherein conversion to bicarbonate and subsequently to CO_2 is sufficiently slow that the risk of hypercapnia is minimized. Acetate dialysis on a sorbent dialysis machine may be preferable for these patients since the nature of the dialysate, which is actually a mixture of acetate and bicarbonate, prevents the bicarbonate loss of single pass acetate dialysis and thus minimizes the amount of acetate transfer (and ultimately CO_2 generation) necessary to correct the patient's acidosis. (Sorbent Dialysis Primer, 1993)

3. Post Open Heart Surgery

Patients with impaired renal function who undergo open heart surgery exhibit a significant degree of both metabolic acidosis and hyperkalemia due to exposure to the cardiopelegia solution used with the pump oxygenator. As a result, acute hemodialysis treatment must be performed either immediately post operatively or, ideally, intraoperatively.

Correction of metabolic acidosis is generally readily achieved by use of a bicarbonate dialysate. Control of hyperkalemia is obtained during the intraoperative dialysis but since potassium tends to rise rapidly during the first 24 post operative hours, redialysis may be necessary during that period (Aguilar, 1983). However, others claim that intra-operative hemodialysis controls the hyperkalemia resulting from the large exogenous and endogenous potassium loads associated with open heart surgry, and redialysis is not necessary during the immediate post operative period (Cardi et al, 1982; Roberts,1984).

There is no difference between sorbent and single pass equipment with respect to application to dialysis of post open heart surgery patients. The advantage of sorbent dialysis in these cases resides in the extreme portability of the equipment, including the lack of water and drain hoses, since the machine must be brought to the patient who is connected to many monitors and other equipment.

* One case report of hypercapnia in a patient on a ventilator dialyzed with the REDY® system has been published (Kidney Int. 21:416, 1982). The dialysis solution utilized contained 135 mmol/liter of sodium bicarbonate, which is no longer recommended. With lower initial dialysis solution concentrations of sodium bicarbonate (100 mmol/liter or below) no confirmatory reports have appeared despite widespread use of the REDY® system in intensive care settings; however, in patients with borderline ventilatory reserve, the blood gases should be monitored closely.

References

Aguilar M, "Case Report of Intraoperative Hemodialysis During Coronary Artery Surgery", *Nephrology Nurse*, pp. 49-53, Nov.-Dec. 1983.

Canzanello V, Rasmussen R, McGoldrick M. "Hyperammonemic Encephalopathy During Hemodialysis", *Ann Intrn Med* 99:190-191, 1983.

Cardi M., Steinman T, Weintraub R, Rosa R, "Intraoperative Hemodialysis During Cardiopulmonary Bypass", *Dialysis & Transplantation*, 11:573 & 576, 1982.

Roberts M, OTC memo, January 18, 1984.

Sorbent Dialysis Primer, 3rd ed., Organon Teknika Corporation, Durham, NC, 1991, pp. 23-25.

SUMMARY

Acute renal failure patients, unstable hospitalized patients with chronic renal failure, and the out-patient on maintenance dialysis with special problems have unique acid/base and electrolyte abnormalities and therefore can best be treated by "Custom Dialysis." Individualized dialysate solutions are readily prepared for the REDY Sorbent System because of its small volume.

The REDY Sorbent System is significantly different from other hemodialysis systems in that the dialysate will equilibrate to the patient's serum level unless additional quantities of the particular solute are added to or removed from the dialysate.

The objectives of hemodialysis are to remove metabolic waste products, normalize the blood pH and electrolyte concentration, and remove excess fluid. The level of waste products in the patient depends upon the efficiency with which they can be removed by hemodialysis as compared to the rate at which they are formed. The blood pH can be normalized by adjusting the bicarbonate level. However, the respiratory function also affects the blood pH and should be taken into consideration in normalizing the pH. Excess fluid can be removed during dialysis or by "sequential ultrafiltration-hemodialysis."

To meet these objectives, the approach has been to formulate three dialysates which increase serum bicarbonate, one which maintains the same serum bicarbonate concentration, and one which reduces the patient's serum bicarbonate. The dialysate which will best normalize the blood pH is selected. The sodium level of the dialysate is adjusted with sodium chloride (see page 27) or water in order to normalize the patient's serum sodium. The removal of fluid during dialysis is facilitated by maintaining the patient hyponatremic between dialyses and using a high sodium and dextrose dialysate plus intravenous albumin. Serum potassium and calcium are adjusted by providing the desired dialysate concentration via the infusate system.

2. CUSTOM DIALYSATES

GENERAL INSTRUCTIONS FOR BICARBONATE DIALYSATES

1. All bicarbonate dialysates in this chapter were devised on the basis that:
   a.) Approximately 16 grams of urea nitrogen will be dialyzed from the patient.
   b.) The infusate provides 6-7 mEq/L of acetate (ex., calcium acetate 3.5 mEq/L, magnesium acetate 1.0 mEq/L and potassium acetate 2.0 mEq/L).
   c.) Dialysis time is 4 hours.
   Significant variation from these conditions may require selection of a dialysate containing more bicarbonate, as discussed in Chapter 1.5 — Special Considerations.
2. We do not recommend the use of chloride infusates with bicarbonate dialysates.
3. For cartridge titration methods only: tap water containing more than 1.0 mEq/L calcium and/or magnesium may turn milky white when bicarbonate is added, due to formation of calcium and/or magnesium carbonates. If this occurs, drain reservoir and use the bicarbonate dialysate purification procedure presented for your machine in Chapter 4.
4. The machine must be put into Cartridge Bypass if dialysis cannot be initiated within 30 minutes after the cartridge is attached, as prolonged recirculation will significantly decrease the concentrations of both sodium and bicarbonate in the dialysate.
5. When initially made, neither bicarbonate nor chloride dialysates contain any potassium, magnesium or calcium. Since approximately 4.5 L of dialysate remains in the reservoir after the cartridge and machine are primed, 11 ml of infusate (2.5 ml x 4.5 L) should be added to bring potassium, magnesium and calcium to prescribed levels prior to patient connection. For the same reason, 2.5 ml infusate should be added to each 1 L of water or sodium adjustment solution used to maintain dialysate conductivity.

All dialysates, dialysate additives, infusates, and infusate additives mentioned in this Guide are available from COBE Renal Care.

Bicarbonate dialysates are also available in KITS. All KITS contain: one pair of non-sterile gloves, one 11 ml syringe, 48g (2 packets) dextrose and acid. Each KIT also contains the following in the quantities indicated:

BICARB KIT 1:	**$NaHCO_3$**	**10 g**
	NaCl	**42 g**
BICARB KIT 2:	**$NaHCO_3$**	**30 g**
	NaCl	**21 g**
	NaCl	**7 g**
BICARB KIT 3:	**$NaHCO_3$**	**50 g**
	NaCl	**14 g**

These KITS have been assembled to correspond with the formulations presented on the following pages. Using a BICARB KIT eliminates the need to titrate bicarbonate dialysate through the sorbent cartridge prior to dialysis.

For a complete listing of all Chemical Packets available from COBE Renal Care, see Appendix 2, Chemicals to Prepare Dialysate, page 51.

If you have any questions please call COBE Renal Care Customer Information Center, Toll Free, at 1-800-456-7339.

MILD ACIDOSIS

BICARB KIT 1

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	20 mEq/L	Sodium	140 mEq/L
NaCl	120 mEq/L	Bicarbonate	10 mEq/L
Dextrose	8 g/L	Chloride	120 mEq/L
		Dextrose	5.7 g/L

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 10 gram packet of $NaHCO_3$
one 42 gram packet of NaCl
two 24 gram packets of dextrose
one bottle of acid (from BICARB KIT)
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.
(3.) Attach prescribed cartridge and infusate to machine.
(4.) Continue set-up procedure according to instructions in Operator's Manual for your machine.
NOTE: It is not necessary to circulate the dialysate through the cartridge for 15 minutes when a BICARB KIT is used.
(5.) Using syringe included in KIT, add 11 ml of infusate to dialysate in reservoir. This will bring dialysate calcium, magnesium and potassium levels to prescribed concentrations.
(6.) Patient may be connected as soon as dialyzer and cartridge are primed.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

MILD ACIDOSIS

CARTRIDGE TITRATION

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	20 mEq/L	Sodium	140 mEq/L
NaCl	120 mEq/L	Bicarbonate	10 mEq/L
Dextrose	8 g/L	Chloride	120 mEq/L
		Dextrose	5.7 g/L

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.

(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.

(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.

(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 10 gram packet of $NaHCO_3$
one 42 gram packet of NaCl
two 24 gram packets of dextrose
DO NOT ADD ACETATE DIALYSATE CONCENTRATE

(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.

(3.) Attach prescribed cartridge. Fill infusate jar with water and attach jar.

(4.) Activate machine and circulate dialysate through cartridge for 15 minutes. The conductivity should drop during the 15 minute titration period. Dialyzer may be set up and primed during circulation period.

(5.) After 15 minute titration period, add 11 ml of infusate solution to the dialysate in the reservoir to bring calcium, magnesium and potassium levels to the prescribed concentrations.
Remove infusate jar containing water and replace with infusate solution prepared in Step B.

(6.) Initiate dialysis within 15-30 minutes after cartridge circulation is begun.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

MODERATE ACIDOSIS

BICARB KIT 2

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	60 mEq/L	Sodium (See NOTE)	140 mEq/L
NaCl	80 mEq/L	Bicarbonate	30 mEq/L
Dextrose	8 g/L	Chloride	80 mEq/L
		Dextrose	5.7 g/L

NOTE – Sodium: Optional NaCl - 7 g. packet. **DO NOT ADD** contents of this packet (step C 1.) if dialysate sodium of 120 mEq/L is prescribed.

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 30 gram packet of $NaHCO_3$
one 21 gram packet of NaCl
one 7 gram packet of NaCl (optional, see note above)
two 24 gram packets of dextrose
one bottle of acid (from BICARB KIT)
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.
(3.) Attach prescribed cartridge and infusate to machine.
(4.) Continue set-up procedure according to instructions in Operator's Manual for your machine.
NOTE: It is not necessary to circulate the dialysate through the cartridge for 15 minutes when a BICARB KIT is used.
(5.) Using syringe included in KIT, add 11 ml of infusate to dialysate in reservoir. This will bring dialysate calcium, magnesium and potassium levels to prescribed concentrations.
(6.) Patient may be connected as soon as dialyzer and cartridge are primed.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

MODERATE ACIDOSIS

CARTRIDGE TITRATION

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	60 mEq/L	Sodium	140 mEq/L
NaCl	80 mEq/L	Bicarbonate	30 mEq/L
Dextrose	8 g/L	Chloride	80 mEq/L
		Dextrose	5.7 g/L

NOTE – Sodium: Optional NaCl - 7 g. packet. **DO NOT ADD** contents during preparation of dialysate (step C 1.) if dialysate sodium of 120 mEq/L is prescribed.

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 30 gram packet of $NaHCO_3$
one 21 gram packet of NaCl
one 7 gram packet of NaCl (optional, see note above)
two 24 gram packets of dextrose
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.
(3.) Attach prescribed cartridge. Fill infusate jar with water and attach jar to machine.
(4.) Activate machine and circulate dialysate through cartridge for 15 minute conductivity should drop during the 15 minute titration period. Dialyzer may be set up and primed during circulation period.
(5.) After 15 minute titration period, add 11 ml of infusate solution to the dialysate in the reservoir to bring calcium, magnesium and potassium levels to the prescribed concentrations. Remove infusate jar containing water and replace with infusate solution prepared in Step B.
(6.) Initiate dialysis within 15-30 minutes after cartridge circulation is begun.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

SEVERE ACIDOSIS

BICARB KIT 3

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	100 mEq/L	Sodium	140 mEq/L
NaCl	40 mEq/L	Bicarbonate	50 mEq/L
Dextrose	8 g/L	Chloride	40 mEq/L
		Dextrose	5.7 g/L

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Sectin 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 50 gram packet of $NaHCO_3$
one 14 gram packet of NaCl
two 24 gram packets of dextrose
one bottle of acid (from BICARB KIT)
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.
(3.) Attach prescribed cartridge and infusate to machine.
(4.) Continue set-up procedure according to instructions in Operator's Manual for your machine.
NOTE: It is not necessary to circulate the dialysate through the cartridge for 15 minutes when a BICARB KIT is used.
(5.) Using syringe included in KIT, add 11 ml of infusate to dialysate in reservoir. This will bring dialysate calcium, magnesium and potassium levels to prescribed concentrations.
(6.) Patient may be connected as soon as dialyzer and cartridge are primed.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

SEVERE ACIDOSIS

CARTRIDGE TITRATION

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Initial Composition (PRE TITRATION)		Patient Exposure (POST TITRATION)	
$NaHCO_3$	100 mEq/L	Sodium	140 mEq/L
NaCl	40 mEq/L	Bicarbonate	50 mEq/L
Dextrose	8 g/L	Chloride	40 mEq/L
		Dextrose	5.7 g/L

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section 2.4.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 50 gram packet of $NaHCO_3$
one 14 gram packet of NaCl
two 24 gram packets of Dextrose
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix by gently rotating six liter jug from side to side until chemicals are dissolved. Do *NOT* shake jug.
(3.) Attach prescribed cartridge. Fill infusate jar with water and attach jar.
(4.) Activate machine and circulate dialysate through cartridge for 15 minutes. The conductivity should drop during the 15 minute titration period. Dialyzer may be set up and primed during circulation period.
(5.) After 15 minutes titration period, add 11 ml of infusate solution to the dialysate in the reservoir to bring calcium, magnesium and potassium levels to the prescribed concentrations. Remove infusate jar containing water and replace with infusate solution prepared in Step B.
(6.) Initiate dialysis within 15-30 minutes after cartridge circulation is begun.
NOTE: Dialysis must be initiated within 30 minutes. If this is not possible, follow General Instruction 4, p. 18.

NORMAL ACID-BASE STATUS AND MILD ALKALOSIS

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION AND PREPARATION

Composition		Patient Exposure	
NaCl	120 mEq/L	Sodium (see note)	120 mEq/L
Dextrose	8 g/L	Chloride	120 mEq/L
		Dextrose	5.7 g/L

NOTE – Add additional 7 g NaCl during dialysate preparation (step C 1.) if a patient sodium exposure of 140 mEq/L is required.

B. ACETATE INFUSATE

Standard Procedure

(1.) Place the contents of a SORB 10 packet in an empty infusate jar.
(2.) Add infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of K-1 increases dialysate potassium by 1.0 mEq/L; each Ca-½ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Directions for preparation of fractional infusates (for example, K = 2.75 mEq/L) are located in Section IV of this chapter.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 42 gram packet of NaCl
two 24 gram packets of dextrose
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix until chemicals are dissolved.
(3.) Attach prescribed cartridge and infusate to machine.
(4.) Continue set-up procedure according to instructions in Operator's Manual for your machine.
NOTE: It is unnecessary to titrate chloride dialysate.
(5.) Patient may be connected as soon as dialyzer is primed.
(6.) Using a syringe, add 11 ml infusate to dialysate in reservoir prior to initiating dialysis. This will bring dialysate calcium, magnesium and potassium levels to prescribed concentrations.

SEVERE ALKALOSIS

IMPORTANT: Read General Instructions on page 18 of this Chapter.

A. COMPOSITION

Composition		Patient Exposure	
NaCl	120 mEq/L	Sodium (see note)	120 mEq/L
Dextrose	8 g/L	Chloride	120 mEq/L
		Dextrose	5.7 g/L

NOTE – Add additional 7 g NaCl during dialysate preparation (step C.1) if a patient sodium exposure of 140 mEq/L is required.

B. CHLORIDE INFUSATE

WE RECOMMEND USE OF CHLORIDE INFUSATES ONLY IN THE TREATMENT OF ALKALOSIS.

Standard Procedure

(1.) Add contents of Chloride infusate packet to empty jar to provide 3 mEq/L Ca and 1 mEq/L Mg in the dialysate.
(2.) Add Chloride infusate additives, if necessary, to attain prescribed levels of dialysate potassium and calcium. The contents of each packet of KCl increases dialysate potassium by 1.0 mEq/L; each $CaCl_2$ increases dialysate calcium by 0.5 mEq/L.
(3.) Fill jar three-fourths full with warm water (110-130°F). Swirl until mixed.
(4.) Add water to neck (300 ml total infusate volume). Mix until dissolved.

Fractional Infusates

Follow instructions under preparation of Fractional Acetate Infusates in Section 2.4 of this chapter except use Chloride Infusate Chemicals.

C. DIALYSATE PREPARATION

(1.) To six liters of water, add the contents of:
one 42 gram packet of NaCl
two 24 gram packets of dextrose
DO NOT ADD ACETATE DIALYSATE CONCENTRATE
(2.) Mix until chemicals are dissolved.
(3.) Attach prescribed cartridge and infusate to machine.
(4.) Continue set-up procedure according to instructions in Operator's Manual for your machine.
NOTE: It is unnecessary to titrate chloride dialysate.
(5.) Patient may be connected as soon as dialyzeris primed.
(6.) Using syringe, add 11 ml infusate to dialysate in reservoir prior to initiating dialysis. This will bring dialysate calcium, magnesium and potassium levels to prescribed concentrations.

IMPORTANT:
It is essential to measure arterial blood gases prior to termination of dialysis and to administer sodium bicarbonate intravenously if the pH has fallen below normal.

2.3. DIALYSATE SODIUM ADJUSTMENT SOLUTION

A. CONCENTRATE
NaCl 720 mEq/L

B. PREPARATION OF CONCENTRATE
(1.) Place into an empty container calibrated at 500 ml, sodium chloride 21 grams.
(2.) Add water to the 500 ml mark.
(3.) Mix until dissolved.

C. PROCEDURE
Add 100 ml to dialysate whenever conductivity drops below desired value.

D. RESULTS
Each 100 ml sodium adjustments solution will add 72 mEq of NaCl to the dialysate. Assuming a 6 liter volume of dialysate, the dialysate sodium concentration will increase by 12 mEq/L and the conductivity will rise approximately 1 mMho.

NOTE: If frequent bath adjustments with water or sodium adjustment solution are necessary to maintain a specific conductivity, machine conductivity should be verified hourly with an independent meter.

2.4. SPECIAL INFUSATES

A. FRACTIONAL INFUSATES
Physicians sometimes order, fractional amounts of potassium in dialysate: A 2.5 mEq/L dialysate, for example. Fractional infusates may be prepared as follows:
1. Dissolve one packet of K-1 infusate additive in 100 ml of warm water.
2. Put desired fraction of the resulting potassium solution in a clean infusate cup. (Example: half of resulting solution equals 0.5 mEq/L potassium additive.)
3. Add the contents of a SORB 10 packet and the desired number of K-1 packets to the cup. (This would be two K-1 packets for our example above.)
4. Fill jar three-fourths full with warm water (110-130°F).
5. Swirl until mixed.
6. Add water to neck (300 ml total infusate volume).
7. Mix until dissolved.

Although the need is less probable, Ca-½ infusate additive may be fractionated in the same manner. In the case of Ca-½ infusate additive, keep in mind that half of the resulting calcium solution prepared in step 1 provides a 0.25 mEq/L Calcium Additive.

NOTE: For severe Alkalosis, use chloride infusate additives.

B. CALCIUM-FREE INFUSATES
Do not use SORB 10. Fill the infusate jar with dialysate from the reservoir to prevent alarms, and attach to machine as usual. The final dialysate will contain no potassium, magnesium or calcium.

If potassium is prescribed, add the contents of the correct number of K-1 infusate additive packets to the empty infusate jar and dilute as usual. The final dialysate will contain potassium but no magnesium or calcium.

The physician must decide whether a magnesium-free dialysate is acceptable. If it is not, add 13 g Magnesium Acetate to the infusate jar for each 1.0 mEq/L of magnesium ordered, and dilute as usual.

If Magnesium Acetate is not available, 12 g Magnesium Chloride may be substituted. Premeasured Magnesium Acetate and Magnesium Chloride packets are available from COBE Renal Care. In an emergency, the hospital pharmacist or crash cart may be able to provide one of these chemicals.

3. ULTRAFILTRATION PROCEDURES

3.1. Ultrafiltration Only
3.2. Sequential Pre-Dialysis Ultrafiltration
3.3. Sequential Post-Dialysis Ultrafiltration

3.1. ULTRAFILTRATION ONLY

1. Set up machine as usual except do not insert cartridge (leave flow line adapter in place).
2. Add 180 ml acetate dialysate concentrate to 6 L water to make dialysate (135 mEq/L sodium). Place in dialysate reservoir.
3. Fill infusate jar with dialysate to prevent infusate alarms. Do not use Sorb 10.
4. Press TREATMENT and then immediately press DIALYZER BYPASS.
5. Set desired value on UF/Negative Pressure Control. Continue treatment until the desired amount of ultrafiltrate is removed.

NOTES: 1. Acetate concentrate is recommended merely as a convenience because it already contains full electrolytes and is easily made. The use of acetate concentrate has no clinical significance in UF Only Procedures. If acetate concentrate is not available, use the Bicarbonate Dialysate mixture recommended in the Pre Dialysis UF Procedure (Bicarbonate Dialysate) on p. 33.

2. If blood leak alarm occurs due to the accumulation of bilirubin and other pigments, replace dialysate.

3.2. SEQUENTIAL DIALYSIS/ULTRAFILTRATION

The two components of the hemodialysis procedure — dialysis (or biochemical exchange) and ultrafiltration — can be applied to the patient's dialyzer separately or simultaneously. Since most hemodialysis patients need both biochemical exchange and fluid removal, the two procedures are normally done simultaneously in order to save time. However, this puts maximal stress on the patient's body, which must then expend considerable energy equilibrating to continuous changes in both its chemical and fluid composition.

While most patients can adapt to the simultaneous procedures, some cannot. This can particularly be a problem for acute dialysis patients, who tend to be both volume overloaded and hemodynamically unstable. Such patients may benefit greatly if the two components of hemodialysis are separated, a procedure known as sequential dialysis/ultrafiltration. Unless the patient has a life-threatening fluid overload, such as frank pulmonary edema, it usually doesn't matter which component is performed first — dialysis or ultrafiltration (UF).

Some practitioners prefer to do the biochemical exchange first. They reason that there is always obligatory UF during the dialysis phase due to the pressure of the patient's venous resisitance against the dialyzer membrane. The amount of this obligatory UF is usually too small (400-600 ml/hr) to cause blood pressure problems but, over a 3-hour dialysis phase, may amount to 1/3-1/2 of the prescribed fluid removal. As a result, the duration of the subsequent UF phase can be shortened accordingly.

Others prefer to do the UF phase first, relying on the patient's undialyzed uremic toxins to maintain his plasma osmolaity and thus vascular refilling rate so that the risk of hypotension during fluid removal is minimized. When the desired volume of ultrafiltrate is obtained, UF is stopped and the dialysis phase begun. Fluid subsequently removed due to the patient's venous pressure (obligatory UF) is replaced by saline infusion on an hourly or half-hourly basis.

Total treatment time is prolonged with either method since no dialysis occurs during the UF phase and the prescription is for duration of dialysis. Methods for performing sequential dialysis/ultrafiltration with REDY® systems are presented on the following pages.

PRE-DIALYSIS ULTRAFILTRATION

ACETATE DIALYSATE

1. Set up machine as usual, including prescribed cartridge, infusate and dialysate.
2. After patient is connected press TREATMENT, then immediately press DIALYZER BYPASS.
3. Set UF control/negative pressure to remove prescribed volume of fluid.
4. When UF Phase is completed, i.e., desired volume removed, release DIALYZER BYPASS to initiate Dialysis Phase.

   If additional UF is desired: Adjust UF control/negative pressure as needed.

   If no further fluid loss is desired: Turn UF control OFF or set negative pressure to a minimum value.

   Note total UF volume obtained. Additional UF will occur due to the effect of the patient's venous resistance on the dialyzer membrane. Note the increase in total UF volume hourly and replace the excess with an equal volume of IV saline.

BICARBONATE DIALYSATE

Clinical Notes:

A. This procedure will provide the same level of acidosis correction as the Bicarb Kit #1 — mild acidosis dialysate formula. For further correction of acidosis, the patient may require additional $NaHCO_3$ via dialysate (5 grams will increase dialysate $NaHCO_3$ level by 10 mEq/L) or IV administration.

B. For treatment of sodium imbalances, procedures for maintenance of a specific conductivity level should be followed. See Section 1.4B, p. 8.

PROCEDURE:

1. Prepare a Bicarb Kit #1 dialysate *except* do not add the 10-gram $NaHCO_3$ to the 6 liters water. *This will be used later.*
2. Set up and prime system as usual using above dialysate, prescribed cartridge, infusate, dialyzer and bloodlines.
3. Connect patient as soon as set-up is complete and satisfactory.
4. Press TREATMENT and DIALYZER BY-PASS.
5. Set required UF value. Continue treatment until the prescribed amount of ultrafiltrate is removed.
6. When UF phase is completed, add the 10-gram $NaHCO_3$ packet from the Bicarb Kit #1 to the reservoir.
7. Release DIALYZER BYPASS to initiate dialysis phase. If additional UF is desired, adjust UF rate as needed. If no further fluid loss is desired, turn UF control off or set negative pressure to a minimum value.

ACETATE OR BICARBONATE DIALYSATE

1. Set up REDY and perform dialysis as usual, except use lowest feasible TMP.
2. At end of desired dialysis period, touch DIALYZER BYPASS control switch.
3. Adjust REDY to achieve desired UF amount.
4. Ultrafiltration period has begun. Discontinue treatment as usual when desired fluid volume has been removed.

4. DIALYSATE PURIFICATION

4.1. WATER QUALITY

As water quality in various parts of the world continues to deteriorate and water quality standards for hemodialysis become more narrowly defined, it may be necessary in some circumstances to pretreat the water used even in sorbent dialysis systems.

Whether pretreatment should be done for a given dialysis depends upon the quality of the tap water available for dialysis and the water quality philosophy adopted by the unit. For example, a different set of standards might be used for acute (temporary) and chronic (permanent) patients.

The following tables are provided to assist in the preparation of dialysate which meets AAMI/ANSI* standards.

The results of routine periodic analysis of available tap water are necessary in order to use the tables. It is suggested that serial analyses be done as water quality in a given area tends to vary considerably over time. It is not necessary to analyze water for all the chemicals listed (the local water district can supply some of the data on a periodic basis, probably free of charge) but items of special interest, such as chloramines, calcium, aluminum, etc., may need to be monitored separately by the dialysis unit.

To use the tables (Figure 4, below), identify the chemical elements of special interest, locate the column that most closely approximates their levels in your tap water and follow the listed recommendations.

Recommendation:

1. If chemical levels are equal to or lower than those listed in the maximum for "STANDARD REDY PREP" column, below, no treatment is necessary. The 15-20 minute recirculation of dialysate which occurs during the standard recommended set-up procedure is adequate to purify dialysate†.
2. If chemical levels exceed the maximum for "STANDARD REDY PREP" but are lower than in the maximum for "REDY PURIFICATION" column, use one of the dialysate purification procedures on pages 38-41.
3. If chemical levels exceed the maximum for "REDY PURIFICATION" column, use purified water (for example, distilled, reverse osmosis or deionized) to make dialysate.

Figure 4: Water Quality

WATER QUALITY CHART

	AAMI/ANSI[1]	REQUIRES STANDARD REDY PREP		REQUIRES REDY PURIFICATION		REQUIRES PURIFIED WATER
SUBSTANCE		MAXIMUM		MAXIMUM		
	mEq/L	mg/L	mEq/L	mg/L	mEq/L	mg/L
Aluminum		0.01		0.03		1.0
Arsenic		0.005		0.015		0.05
Barium		0.1		0.3		1.0
Calcium[2]	0.1	2.0	4.5	90.0	7.2	145.0
Cadmium		0.001		0.003		0.01
Chlorine		0.5		1.5		6.0
Chloramines		0.1		0.3		6.0
Chromium		0.014		0.042		0.7
Copper		0.1		0.3		0.5
Fluoride		0.2		0.6		2.0
Lead		0.005		0.015		0.05
Magnesium[2]	0.3	4.0	2.0	24.0	3.3	40.0
Mercury		0.0002		0.0006		0.002
Nitrate		2.0		2.0		2.0
Postassium[2]	0.2	8.0	0.5	20.0	1.5	60.0
Selenium		0.09		0.27		0.9
Silver		0.005		0.015		0.05
Sodium[3]	3.0	70.0	3.0	70.0	3.0	70.0
Sulfate		100.0		100.0		100.0
Zinc		0.1		0.3		1.0
Bacteria		200/ml		600/ml		2000/ml

[1]Based in part on the AAMI/ANSI recommended Standards for water used to make hemodialysate, August, 1982.
[2]Sorbent Cartridges completely remove these substances. They are then replaced at the desired level by the infusate system.
[3]The volume of concentrate added to the six liters of water should be adjusted to compensate for the presence of sodium in tap water.

*Association for the Advancement of Medical Instrumentation/American National Standards Institute, Inc.

†Except Ca and Mg

4.2. CHLORAMINE REMOVAL

ACETATE, CHLORIDE OR BICARBONATE DIALYSATES

RAPID DIALYSATE PURIFICATION – CHLORAMINE REMOVAL ONLY

A. Prepare dialysate using six liters of warm water* in jug provided with machine.
B. Add Ascorbic Acid (see NOTE below) to dialysate mixture in six liter jug. Swirl fluid in jug briefly to mix.
C. Insert cartridge as usual. Fill infusate jar with prescribed infusate mixture and connect to machine. (IMPORTANT: the pH of bicarbonate dialysate must be adjusted before initiating infusate flow. Use acidifier from Bicarb Kit or cartridge titration method.)
D. Pour contents of jug into dialysate reservoir. Start flow of dialysate through cartridge as usual. Dialyzer may be primed and dialysis initiated at user's convenience.

NOTE: One Ascorbic Acid packet is sufficient to remove up to 10 mg/L of chloramines from 6 L of dialysate. The premeasured Ascorbic Acid (180 mg) is packaged with a small amount of dextrose (4 gm) which serves as a blending agent. The amount of dextrose in the final six liters of dialysate is negligible (0.67 gm/L) and will neither harm nor benefit the patient.

*Meets REDY PREP standards, except for chloramines. By Federal standards maximum chloramine level allowed in tap water is 10 mg/L.

4.3. PURIFICATION METHOD

ACETATE OR CHLORIDE DIALYSATES

Purpose: To remove aluminum, chloramines, and other undesirable elements from dialysate made with chemically impure but potable tap water.

Extra Material Needed:
Purification Adaptor, which consists of a cartridge connector with 3 feet ¼" O.D. PVC tubing attached. These materials can be purchased from COBE Customer Service Department, (1-800-525-2623).

Procedure:

1. Prepare dialysate in 6 L jug provided with the REDY (Note 1).
2. Place cartridge and infusate on machine as usual.
3. Turn power ON. Sequence system to "SYSTEM READY". Add dialysate to reservoir. Place 6 L jug next to machine.
4. In place of usual connector at top of cartridge, insert the Purification Adaptor with open end of tubing going into 6 L jug.
5. Press STANDBY; system will go into its priming sequence.
6. Meanwhile, set-up dialyzer and blood lines; perform saline prime as usual.
7. Collect purified cartridge effluent in 6 L jug until reservoir is low. Reservoir will not completely empty; jug will contain about 4 L of fluid.
8. Drain unprocessed fluid from reservoir; turn power OFF.
9. Restart system and pour purified dialysate accumulated in jug into machine reservoir.
10. Add 9 ml of infusate to reservoir to provide prescribed amount of calcium, magnesium, and potassium.
11. Remove Purification connector from top of cartridge and replace with cartridge connector on REDY SYSTEM.
12. Connect dialysate lines to dialyzer.
13. Press STANDBY.
14. System is ready for dialysis.

NOTES: 1. Use this procedure on acetate or chloride dialysates only. Do not use on bicarbonate dialysate. Do not use these procedures to purify tap water as damage to the sorbents in the cartridge will result.

4.4. PURIFICATION METHOD

BICARBONATE DIALYSATE

BICARB KITS

General Method:
Sorbent bicarbonate dialysate "concentrate" consists of two chemicals, NaCl and $NaHCO_3$. The bicarbonate purification procedure involves purifying a mixture of NaCl in six liters of water first, then adding the $NaHCO_3$. The NaCl must be added to the water because plain tap water will damage the cartridge. The $NaHCO_3$ must be added after the purification is accomplished because too much of it will be coverted into CO_2 gas — and lost to the atmosphere — if it is "single passed" through the cartridge with the NaCl and water.

Extra Materials Needed:
Purification Adaptor, which consists of a cartridge connector with 3 feet ¼" O.D. PVC tubing attached. These materials can be purchased from COBE Customer Service Department.

Procedure:

1. Mix the prescribed amount of NaCl with 6 liters warm water in the jug provided with the REDY® system.
2. Place cartridge and infusate on machine as usual. In place of usual connector at top of cartridge, insert the purification adaptor.
3. Turn power ON. Pour contents of jug into reservoir and place empty jug next to machine. Put open end of purification adaptor tubing into jug. (Fig. 5)
4. Press STANDBY. System will begin priming.
5. Set up dialyzer and blood lines; perform saline prime as usual.
6. Collect purified cartridge effluent in 6-liter jug until jug contains at least 4.0 liters of fluid, then drain any unprocessed fluid from reservoir and turn power off.
7. Remove purification adaptor from top of cartridge and replace with cartridge connector on REDY® system.
8. Add prescribed amounts of $NaHCO_3$, dextrose and acid to fluid accumulated in jug, swirl contents to mix.
9. Restart system and pour contents of jug into machine reservoir.
10. Add 10 ml of infusate to reservoir to provide prescribed amount of calcium, magnesium, and potassium. Stir briefly with any clean plastic implement to mix.
11. Activate DIALYZER BYPASS, connect dialysate lines to dialyzer, press STANDBY to deactivate bypass. System is ready for dialysis. (See NOTE)

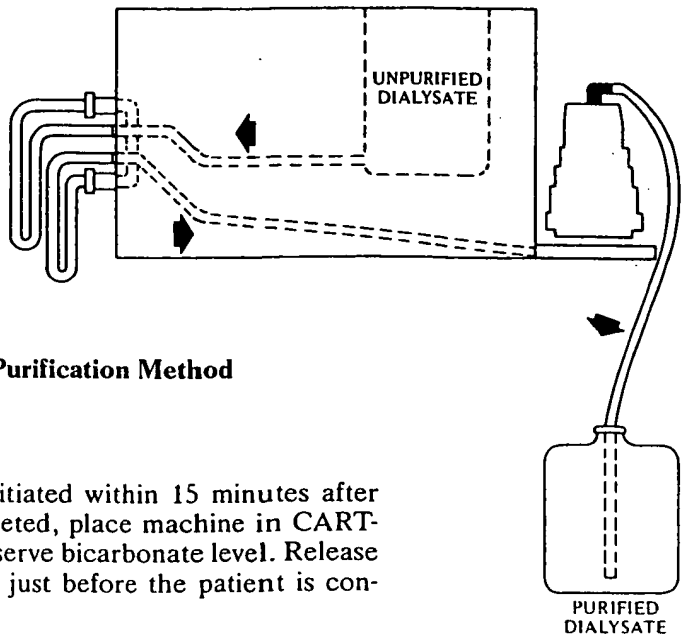


Figure 5: Dialysate Purification Method

NOTE: If dialysis cannot be initiated within 15 minutes after machine setup is completed, place machine in CARTRIDGE BYPASS to preserve bicarbonate level. Release CARTRIDGE BYPASS just before the patient is connected.

4.4. PURIFICATION METHOD

BICARBONATE DIALYSATE

CARTRIDGE TITRATION

General Method:
Sorbent bicarbonate dialysate "concentrate" consists of two chemicals, NaCl and $NaHCO_3$. The bicarbonate purification procedure involves purifying a mixture of NaCl in six liters of water first, then adding the $NaHCO_3$. The NaCl must be added to the water because plain tap water will damage the cartridge. The $NaHCO_3$ must be added after the purification is accomplished because too much of it will be coverted into CO_2 gas — and lost to the atmosphere — if it is "single passed" through the cartridge with the NaCl and water.

Extra Material Needed:
Purification Adaptor, which consists of a cartridge connector with 3 feet ¼" O.D. PVC tubing attached. These materials can be purchased from COBE Customer Service Department.

Procedure:

1. Mix the prescribed amount of NaCl with 6 liters warm water in the jug provided with the REDY® system.
2. Fill the infusate jar with water and connect to the machine. Place cartridge on machine but replace usual connector at top of cartridge with the purification adaptor.
3. Turn power ON. Pour contents of jug into reservoir and place empty jug next to machine. Put open end of purification adaptor tubing into jug. (Fig. 5)
4. Press STANDBY. System will begin priming.
5. Set up dialyzer and blood lines; perform saline prime as usual. Mix prescribed infusate and set aside.
6. Collect purified cartridge effluent in 6-liter jug until at least 4 liters have been collected, then drain any unprocessed dialysate from reservoir and turn power OFF.
7. Remove purification adaptor from top of cartridge and replace with cartridge connector on REDY® system.
8. Add prescribed amount of $NaHCO_3$ and dextrose to fluid in 6-liter jug. Swirl contents to mix.
9. Restart system and pour contents of jug into machine reservoir.
10. Allow dialysate to recirculate for 15 minutes.
11. At the end of recirculation period, connect prescribed infusate to the infusate system in place of water. Add 10 ml of infusate to reservoir to provide prescribed amounts of calcium, magnesium, and potassium to initial dialysate.
12. Activate DIALYZER BYPASS, connect dialysate lines to dialyzer, deactivate DIALYZER BYPASS. System is ready for dialysis. (See NOTE)

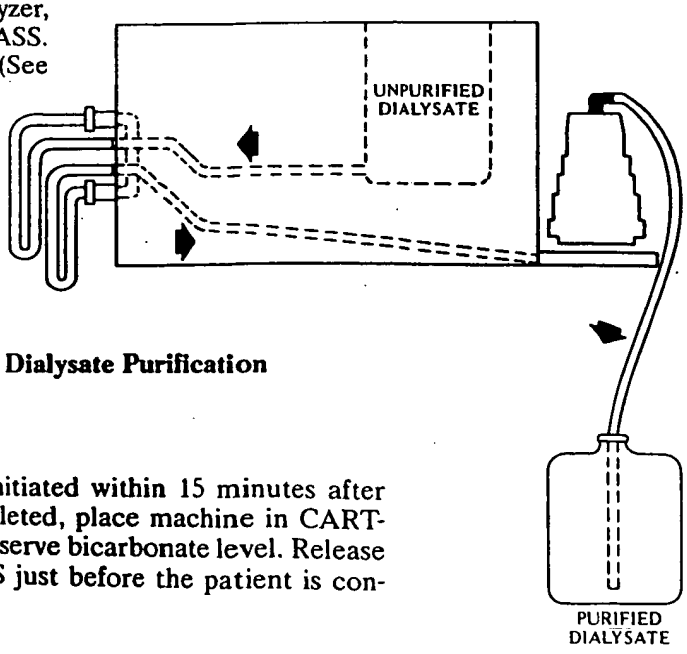


Figure 5: Bicarbonate Dialysate Purification

NOTE: If dialysis cannot be initiated within 15 minutes after machine setup is completed, place machine in CARTRIDGE BYPASS to preserve bicarbonate level. Release CARTRIDGE BYPASS just before the patient is connected.

5. DRUG OVERDOSE

5.1. INTRODUCTION

The overall mortality from poison and drug overdose is very low, less than 2.3%.[1] This is due to the fact that most patients are not severely poisoned and receive intensive supportive care. Prompt institution of measures designed to prevent circulatory and respiratory insufficiency remain the fundamental therapeutic approach to the treatment of drug poisoning. Additional measures, such as gastric lavage, forced diuresis, and administration of pharmacologic antagonists or oral sorbents, may be added to the treatment regimen in some cases. The vast majority of poisoned patients respond to these conservative measures.

However, the mortality of patients in Stage IV Coma is still appreciable, ranging from 5-34%.[2] In these cases extracorporeal therapy, such as hemodialysis, hemoperfusion or plasmapheresis may be considered as an adjunct to intensive supportive therapy.

Hemodialysis may be selected as the treatment of choice for one or more of the following reasons:

1. The poison is not as effectively removed by other treatment modalities.
2. It is necessary to correct drug-induced acid-base or electrolyte abnormalities in addition to removing the substance itself.
3. Other extracorporeal treatment modalities are not readily available and/or practicable.

In order to remove a poison or drug by hemodialysis, the substance must be dialyzable. Thus identification of the substance or substances involved is highly desirable, although not always possible. Specific identification permits such factors as the molecular weight and pharmacokinetic characteristics of the substance (volume distribution, protein binding, lipid solubility, etc.) to enter into the decision of whether, how and how often hemodialysis should be performed. A list of dialyzable poisons and drugs is given in this Section on page 48.

Once the decision to use hemodialysis is made, the following procedure guidelines are generally employed:

1. A large surface area dialyzer with highly permeable membrane is used, if available.
2. Dialysis time is increased. In many cases, the patient is dialyzed until consciousness returns.
3. A customized dialysate is often required, since the fluid, electrolyte and acid-base status of such patients often differ considerably from each other (as well as from that of the usual renal patient).

5.2. USE OF SORBENT DIALYSIS IN DRUG OVERDOSE

In the case of sorbent dialysis systems, the molecular weight of the known or suspected poison is a useful determinant in the decision as to whether to perform a conventional sorbent dialysis, using the cartridge to adsorb the toxin(s) from the spent dialysate, or to convert the system to a single-pass mode for the purpose of removing solutes which are not readily adsorbed.

In general, substances that are not well removed by the sorbents in hemoperfusion columns are not effectively removed by the sorbents in the SORB Cartridge. Specifically, most low molecular weight substances are not adsorbed well. Chief among those substances seen in overdose situations that are poorly adsorbed by sorbents are the alcohols: methanol, ethanol, isopropanol and ethylene glycol. Sorbent dialysis systems should be used in the single-pass mode for treatment of poisoning by these and other low molecular weight solutes.

Substances such as low molecular weight hydroxy and amino compounds, known not to be significantly adsorbed by sorbent cartridges are indicated in the drug list, adapted from Winchester,[3] provided on page 48. Also indicated on the list are those substances which are known to be adequately adsorbed by the cartridges.

However, it is not feasible to test every known substance for adequacy of adsorption by the sorbent cartridge. When in doubt, the effluent from the cartridge should be tested and the cartridge changed, if the substance is present in the effluent at too high a concentration to provide an effective gradient.

The following chart has been prepared as a general guideline to assist in determining whether a conventional sorbent or a single-pass mode is appropriate in a given situation.

Figure 6: Overdose Guidelines

DRUG	PROCEDURE
MW>100	
A. Known to be adsorbed by cartridge	Use conventional sorbent dialysis procedure. Change cartridge if necessary (each cartridge will bind about 5 gm of drug).
B. Adsorption unproven (MW>100 = high probability of adsorption)	Use conventional sorbent dialysis procedure. Test cartridge effluent every hour for presence of drug(s).
MW<100	
C. Known or suspected not to be adsorbed	Use Single Pass Mode (Acetate Bath). Do not use cartridge or infusate.* Change dialysate every 30 minutes.

*Put dialysate in infusate jar

Specific procedures for using sorbent dialysis systems in both conventional and single-pass modes for the treatment of drug overdose are outlined in the next section.

REFERENCES

[1]Bly, E., Lorch, J., and Cortell, S., "Extracorporeal Therapy in the Treatment of Intoxication", *American Journal of Kidney Diseases,* Vol. III, No. 5, March 1984, p. 321.

[2]Winchester, J., "Poisoning — Active Treatment Methods", *Dialysis & Transplantation,* 13:1, January 1984, p. 21.

[3]Winchester (IBID, p. 25), used with permission.

SEE ALSO: Haddad, L.M., and Winchester, J.F., *Clinical Management of Poisoning and Drug Overdose,* 2nd Ed., W.B. Saunders Company, Philadelphia, 1990.

Davidson, W. "Hemodialysis and Hemoperfusion in the Management of Acute Drug Intoxication". In: Massry, S., Glassock, R.J. (Eds.) *Textbook of Nephrology,* 2nd Ed., Williams & Wilkins, Baltimore, 1989, pp. 1565-1570.

Feinstein, E. "Acute Drug Intoxification". In Glassock, R.J. (Ed.) *Current Therapy in Nephrology & Hypertension,* 3rd Ed., Decker-Mosby, St. Louis, 1992, pp. 246-251.

5.3. OVERDOSE PROCEDURES

A. Conventional Sorbent Dialysis

1. Set up machine as per instructions in Operator's Manual.
2. Prepare an acetate dialysate (one package of Dry Acetate* dialysate chemicals *or* 135 ml of any standard dialysate concentrate added to 6 liters of warm, potable water).
   NOTE: If the patient is hyponatremic, prepare initial dialysate with a sodium of 135-145 mEq/L. (Add 200 ml sodium adjustment solution to one package of dry acetate dialysate chemicals in 5.8 L warm potable water for a total volume of 6 L *or* add 180-190 ml acetate dialysate concentrate to 6 L warm potable water).
3. SORB Cartridges have a drug adsorption capacity of approximately 5 grams. There is no difference, in this respect, between SORB (641207-000) and HiSORB (641208-000) Cartridges. Either may be used.
4. The pharmacokinetics of the drug involved and characteristics of the dialyzer membrane are the main determinants of how much drug will enter the dialysate and thus be presented to the SORB Cartridge during the procedure. Although the capacity of the cartridge is comparatively large, it is recommended that:
   a. The drug level of the cartridge effluent (fluid coming out of the top of the cartridge) be examined every 1-2 hours, if possible. If concentration of drug in the cartridge effluent sample is significant, cartridge should be promptly replaced.
   b. The cartridge be changed every four hours.

*Available from COBE Renal Care

5. Monitor the patient's acid-base status periodically throughout the procedure. Many poisoned patients are acidotic and most are not uremic. Since the amount of organic base in the initial dialysate is not large and the non-uremic patient will not stimulate significant bicarbonate production from the cartridge during the procedure, adequate correction of acidosis, if present, will not occur. Thus the need for IV bicarbonate supplementation is probable. ***Use of a bicarbonate dialysate will not alter the need for IV bicarbonate supplementation.***

B. Conversion to Single-Pass Mode

1. Set up system as per Operator's Manual, except:
   a. Do not use sorbent cartridge. Leave cartridge Bypass tube in place.
   b. Do not use infusate. Fill infusate jar with dialysate and connect to system as usual.
2. Unless directed otherwise by the physician, prepare dialysate with a sodium of 135-145 mEq/L. Acetate-based dialysate is easiest to use. To make a 135-145 mEq/L sodium dialysate, use ONE of the following methods.
   a. Add 200 ml sodium adjustment fluid, Chapter 2.3. p. 27, to one package of Dry Acetate Dialysate dissolved in 5.8 L, warm (38°C) potable water, for a total volume of 6 L.
   b. Add 180-190 ml liquid acetate dialysate concentrate to 6 L warm (38°C) potable water.
3. Initiate dialysis. Physician should evaluate the possible need for serum potassium repletion (IV or via dialysate) during the dialysis.
4. Replace dialysate every 30 minutes in order to maintain maximum concentrate gradient.
   a. Drain reservoir until low reservoir volume (LO VOL) alarm occurs (REDY 2000) or reservoir is empty.
   b. Add 6 L of fresh dialysate to reservoir. Use one of the dialysates listed in Step 2, above.
   c. Continue treatment.

5.4. DRUGS REMOVED BY HEMODIALYSIS

Drugs Preferably Removed by Hemodialysis[1]

ALCOHOL[3]
- Ethanol[3]
- ethylene glycol[3]
- methanol[3]

ANALGESICS
- acetaminophen
- acetylsalicylic acid[2]
- methylsalicylate[2]
- salicyclic acid[2]

ANTIDEPRESSANTS
- amphetamine
- methamphetamine

ANTIMICROBIALS/ ANTI-CANCER AGENTS[4]
- amikacin
- ampicillin
- azathioprine
- aziocillin
- bacitracin
- cafamandole
- carbenicillin
- cephaloridine
- cephalothin
- cloramphenicol
- chloroquine
- colchicine
- colistin
- (cyclophosphamide)
- (cycloserine)
- (ethambutol)
- 5-fluorouracil
- flucytosine
- fosfomycin
- gentamicin
- (hexachlorophene)
- (isoniazid)
- kanamycin
- (methatrexate)
- nafcillin
- neomycin
- nitrofurantoin
- penicillin
- polymyxin
- quinine
- streptomycin
- sulfonamides
- tetracycline
- tobramycin
- vancomycin

BARBITUATES[2]

METALS/INORGANICS
- arsenic[2]
- borates
- boric acid
- bromide[3]
- fluoride[2]
- lead[2]
- lithium[3]
- phosphate[2]
- potassium[2]
- sodium[3]

NONBARBITURATE HYPNOTICS, SEDATIVES, AND TRANQUILIZERS
- carbamazepine
- carbromal
- chloral hydrate
- chlordiazepoxide
- chlorpromazine
- (diazepam)
- diethylpentenamide
- diphenhydramine
- ethchlorvynol
- glutethimide
- (heroin)
- meprobamate
- methaqualone
- methsuximide
- methyprylon
- paraldehyde
- primidone

PLANT/ANIMAL TOXINS, HERBICIDES, AND INSECTICIDES
- methyl mercury complex

SOLVENTS/GASES
- acetone[3]
- camphor[2]

CARDIOVASCULAR AGENTS
- methyldopa
- practolol
- propranolol

MISCELLANEOUS
- cimetidine
- methyl mercury comp
- methylprednisolone oxalate[2]
- oxalic acid[2]
- sodium citrate[3]
- theophylline[2]

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[1]From: Winchester, J. F., "Poisoning — Active Treatment Methods," *Dialysis & Transplantation.* 13:21-26. 1984. For additional information see: Haddad, L. M., Winchester, J. F., eds. *Clinical Management of Poisoning and Drug Overdose,* Philadelphia: W. B. Saunders Co., 1990.

[2]Substances known to be adsorbed by the sorbent cartridge. Barbiturates are also adsorbed by the cartridge from the dialysate. However, Winchester recommends that these drugs be removed from the patient by hemoperfusion. Because of the thousands of substances which can cause poisioning, it is not possible to test the sorbent cartridge for each substance.

[3]Substances known not to be significantly adsorbed by the sorbent cartridge — change dialysate frequently. See page 47, procedure 5.3B, for method.

[4]Many drugs in this category have not been studied with hemoperfusion as a possible better technique.

( ) Not well removed by hemodialysis or hemoperfusion.

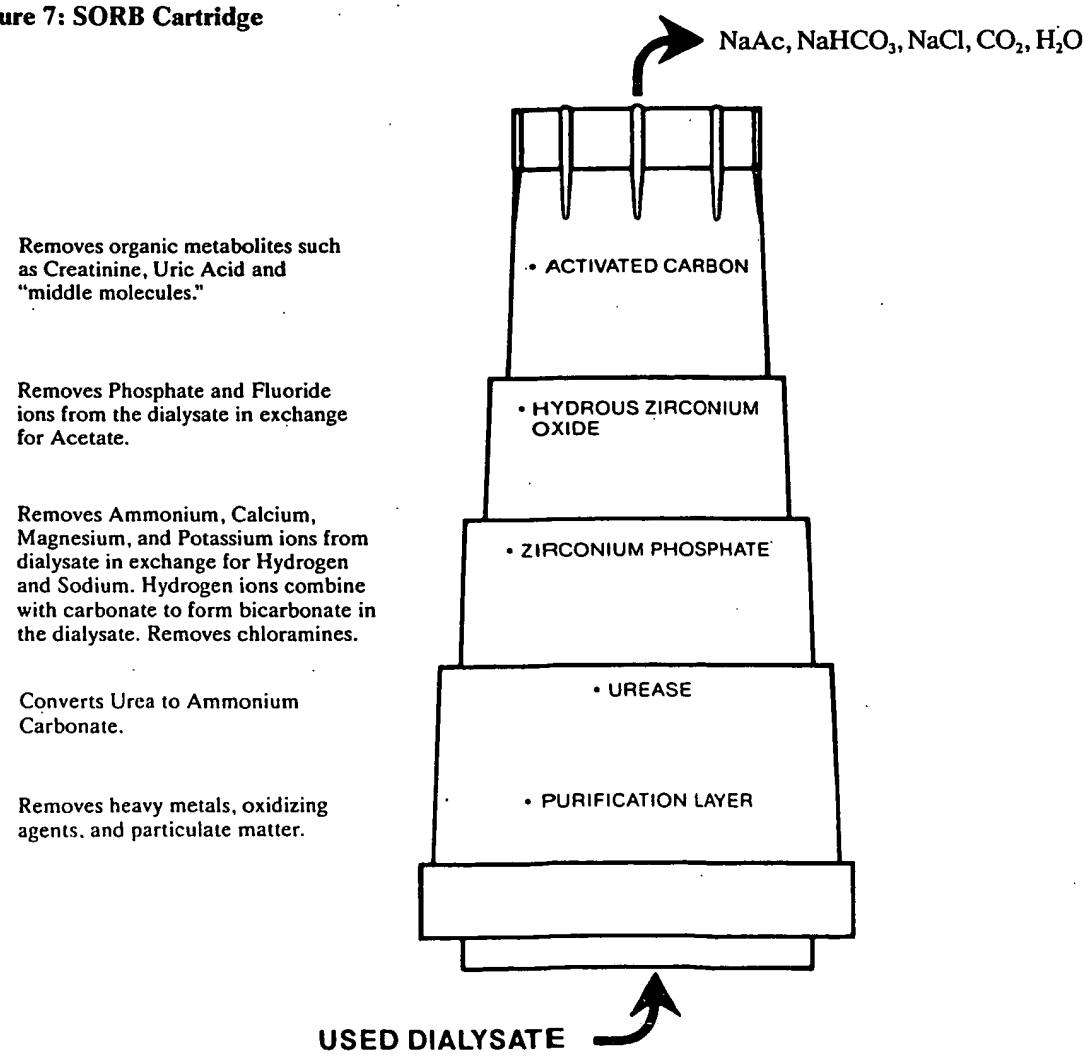
1. Sorbent Cartridge
2. Chemicals to Prepare Dialysate
3. Calculations and Formulas

1. SORBENT CARTRIDGE

A. Composition

1. Purification Layer
   The first layer is the purification layer, consisting of activated carbon. This layer removes heavy metals and oxidizing substances possibly present in the water used to prepare the dialysate.
2. Urease Layer
   Urease is an enzyme which converts urea to ammonium carbonate.
3. Zirconium Phosphate Layer
   Zirconium phosphate, a cation exchanger, is present in the sodium and hydrogen forms. Cations such as potassium, calcium, magnesium, and ammonium are exchanged for sodium and hydrogen ions, the ratio depending upon the pH of the zirconium phosphate and whether the cation is associated with a weak or strong acid anion. Chloramines are also adsorbed by this layer.
4. Hydrated Zirconium Oxide Layer
   Zirconium oxide is an anion exchanger provided in the acetate form, but is converted to the bicarbonate form in the presence of the bicarbonate dialysate. Anions such as phosphate and fluoride are exchanged for acetate or bicarbonate.
5. Activated Carbon Layer
   Activated Carbon adsorbs organic metabolites such as creatinine, uric acid, and "middle molecules". Low molecular weight hydroxy and amino compounds such as methyl and ethyl alcohol, glucose, and glycine are poorly adsorbed.

Figure 7: SORB Cartridge



B. Capacity

The capacity of the cartridge to adsorb the ammonium ion created by the hydrolysis of urea is limited by the capacity of the zirconium phosphate. The amount of urea nitrogen in grams to be removed from the patient can be estimated by multiplying the expected drop in SUN in gm/kg by the calculated body fluid in liters (60 to 70% of total body weight in kilograms). (See Appendix 3, D.).

1. SORB Cartridge (641207-000): This cartridge has a maximum urea nitrogen capacity of 20 grams.
2. HiSORB Cartridge (641208-000): This cartridge has a maximum urea nitrogen capacity of 30 grams:

2. CHEMICALS TO PREPARE DIALYSATE

The following chemical packets are available from COBE Renal Care:		**PRODUCT NO.**
BICARB KITS		
Bicarb Kit 1 (20 per case)	Details on	635640-000
Bicarb Kit 2 (20 per case)	page 16	635641-000
Bicarb Kit 3 (20 per case)		635642-000
DIALYSATE CONCENTRATE (ACETATE)		
Dry Acetate Concentrate (20 per case)		635633-000
Sodium Acetate	15 grams	
Calcium Acetate	1.6 grams	
Sodium Chloride	26 grams	
Magnesium Acetate	0.6 grams	
Potassium Acetate	0.6 grams	
DIALYSATE CONCENTRATE (SODIUM BICARBONATE)		
$NaHCO_3$ (10 g, 40 per case)		635634-000
$NaHCO_3$ (30 g, 40 per case)		635635-000
$NaHCO_3$ (50 g, 40 per case)		635636-000
DIALYSATE CONCENTRATE (SODIUM CHLORIDE)		
NaCl (14 g, 40 per case)		635637-000
NaCl (21 g, 40 per case)		635638-000
NaCl (42 g, 40 per case)		635639-000
DIALYSATE ADDITIVES		
$NaHCO_3$ (5 g Sodium Bicarbonate, 40 per case)		635643-000
NaCl (7 g Sodium Chloride, 40 per case)		641901-000
Dextrose (24 g, 120 per case)		635644-000
Ascorbic Acid (180 mg, 120 per case)		635645-000
INFUSATES		
SORB 10 (20 per case)		641213-000
Chloride Infusate (MgCl:12 g and $CaCl_2$:26 g, 40 per case)		635648-000
INFUSATE ADDITIVES		
K-1 (12 g, 120 per case)		652076-000
Ca-½ (5 g, 40 per case)		635649-000
Mg Acetate (13 g, 40 per case)		635653-000
KCl (9 g, 40 per case)		635651-000
$CaCl_2$ (4 g, 40 per case)		635652-000
MgCl (12 g, 40 per case)		635654-000
DECALCIFYING AGENTS		
Citric Acid (300g, 20 per case)		607120-000

3. CALCULATIONS AND FORMULAS

A. Sodium Bicarbonate

Approximately 15% of the urea passing through the sorbent cartridge is converted to sodium bicarbonate.

Example: 17 grams of urea-nitrogen is converted to 182 mEq of sodium bicarbonate

$$\frac{\text{17 grams urea-nitrogen}}{\text{14 grams/mole}} \times 0.15 \times 1000 = 182 \text{ mEq of sodium bicarbonate}$$

Where:

17 grams urea-nitrogen is the assumed amount of urea-nitrogen adsorbed by the cartridge (see Appendix 3, D.); 14 grams/mole is the formula weight of nitrogen; 0.15 is the average percent conversion of urea to sodium bicarbonate by the cartridge; and 1000 is the conversion of Eq to mEq.

B. Sodium Acetate

Calcium, magnesium, and potassium acetates are converted to sodium acetate when passed through the sorbent cartridge.

Example: An infusate providing 3.5 mEq/L calcium, 1 mEq/L magnesium acetate and 2 mEq/L potassium acetate when passed through a sorbent cartridge during 4 hours of dialysis at a dialysate flow of 200 ml/min.

6.5 mEq/L x 200 ml/min x 0.001 x 60 min/hr x 4 hr = 312 mEq

Where:

6.5 mEq/L is the total mEq of acetate from calcium, magnesium, and potassium acetates; 200 ml/min is the dialysate flow rate; 0.0001 is the conversion from milliliters to liters; and 60 min/hr is the conversion from minutes to hours.

C. Potassium

1. An increase in pH of 0.1 units will decrease the serum potassium by 0.6 mEq/L.
   Example: The pH of the patient was increased from 7.32 to 7.42. The serum K+ will decrease 0.6 mEq/L unless adjusted during the dialysis.
2. A decrease in pH of 0.1 units will increase the serum potassium by 0.6 mEq/L.
   Example: The patient's alkalosis was partially corrected by dropping the pH from 7.56 to 7.45. The serum potassium will increase 0.6 mEq/L unless adjusted during dialysis.

D. Cartridge Capacity

The capacity of the sorbent cartridge is limited by the amount of ammonia which can be adsorbed by the zirconium phosphate. This, in turn, limits the capacity of the cartridge for urea. The SORB (641207-000) Cartridge has a maximum urea-nitrogen capacity of 20 grams while the HiSORB has a maximum urea-nitrogen capacity of 30 grams. Which cartridge to use can be determined by calculating the estimated urea-nitrogen to be adsorbed by the cartridge.

Example: A patient has a body weight of 70 kg and a serum urea-nitrogen of 80 mg/dl. Considering factors such as dialyzer clearance, dialysis duration, blood and dialysate flow rates, it is estimated that the SUN will be 45 mg/dl at the end of dialysis.

The formula for the calculation to determine which cartridge to be used is:

Expected drop in SUN (g/L) x Body Fluid Volume (kg)

1. Expected drop in SUN.
   To convert mg/dl (or mg%) to g/L, move the decimal point 2 places to the left. Thus, 80 mg/dl - 45 mg/dl = 35 mg/dl or 0.35 g/L
2. Body Fluid Volume = Body Weight in kg x % Body Water
   Assuming this patient's body fluid volume comprises 60% of body weight,
   70 kg x 0.6 = 42 kg = 42 L
3. Multiply the two results. 0.35 g/L x 42 L = 14.7 g

Therefore, a SORB (641207-000) Cartridge will be adequate.

NOTE: Prolonged recirculation of dialysate will reduce cartridge capacity for ammonia; approximately 1 gram of capacity will be lost every 40 minutes of recirculation. In addition, prolonged recirculation will reduce the amount of bicarbonate in the initial dialysate. For these reasons we recommend the machine be turned off or placed in STANDBY/CARTRIDGE BYPASS mode if dialysis cannot be initiated within 15 minutes after set-up is completed.